GI Polyps and polyp-like lesions

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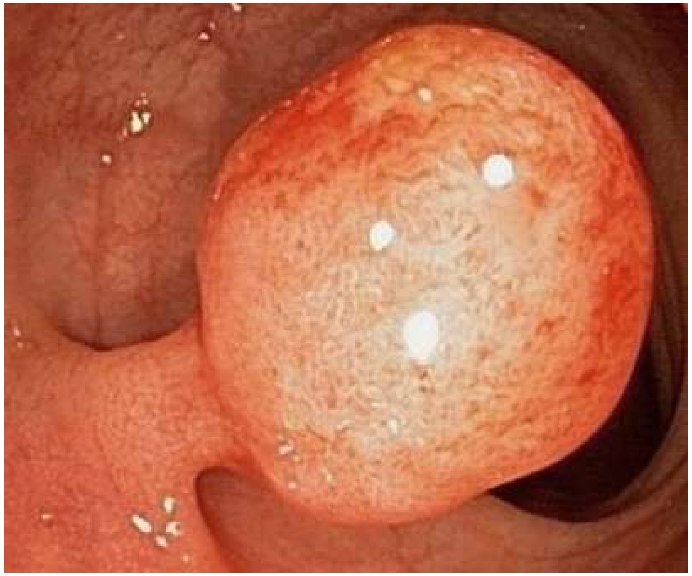
Polyp

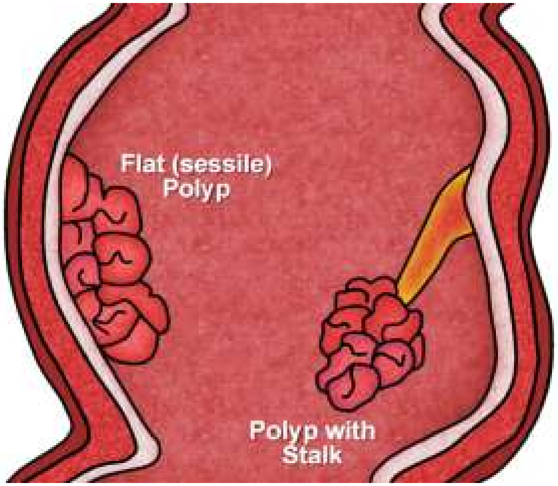
Tumor or tumor-like lesion

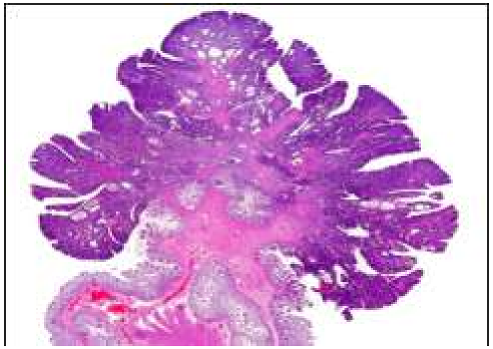
Protrudes above an epithelial surface

Narrow-based with a pedicle (pedunculated)

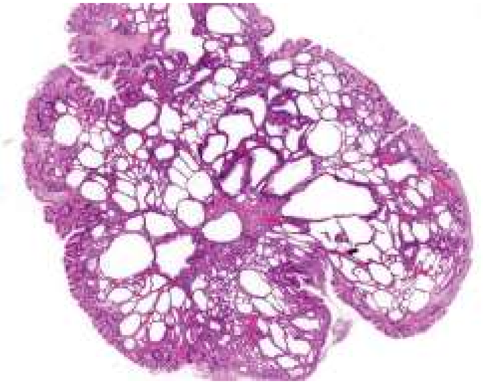
Broad-based with no pedicle (sessile)



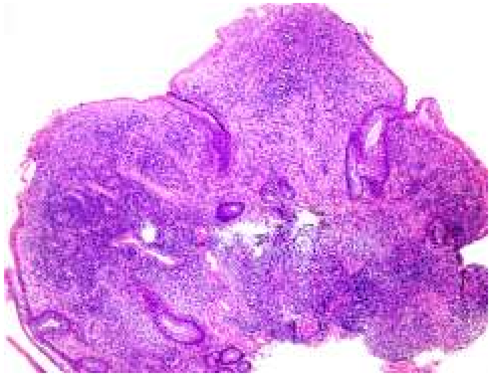




Neoplastic



Hamartomatous



Inflammatory

Polyps

Polyps can be **asymptomatic** or cause **bleeding** (surface ulceration), **pain** (torsion or intussusception) or other symptoms depending on location

Classified as **neoplastic, hamartomatous, inflammatory, regenerative, other types**

Majority of polyps are **benign** but some can **progress to cancer**

Most polyps are **sporadic** but some are **multiple** (heritable cancer syndromes)

Some neoplasms (benign or malignant) may have polypoid outlines

Polyps of the esophagus

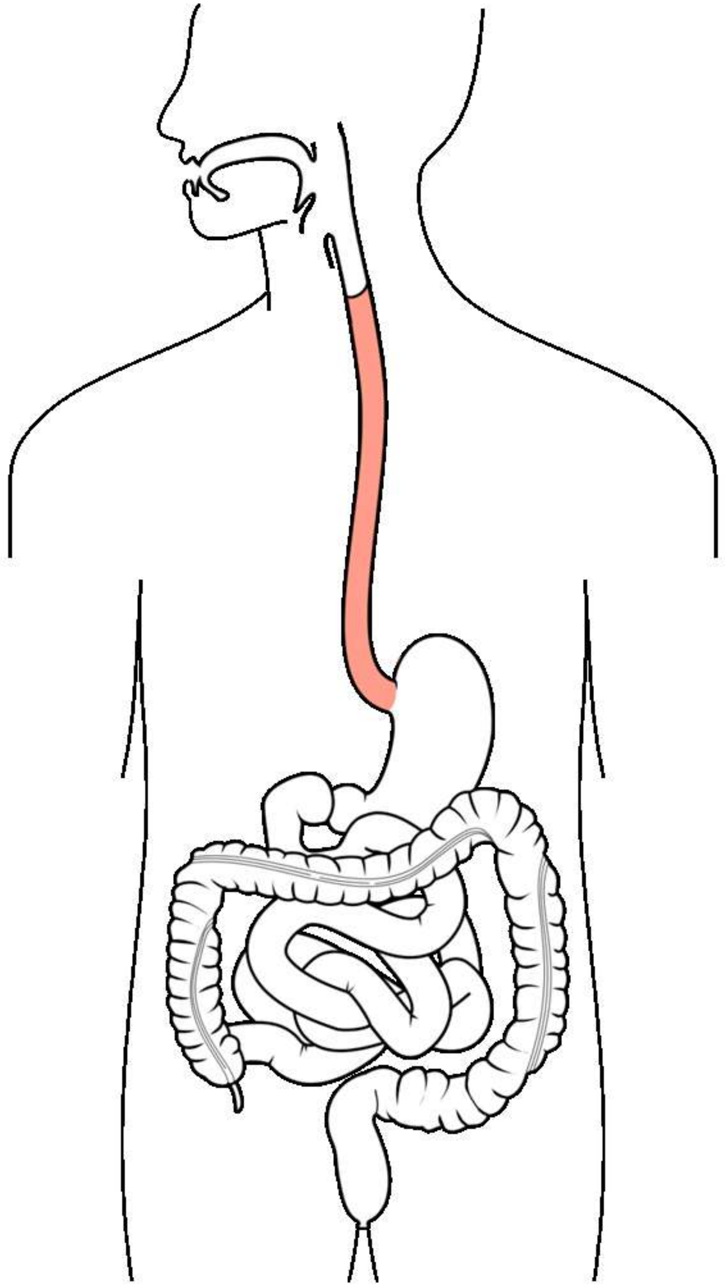
Squamous papilloma

Fibrovascular/fibroepithelial polyps

Inflammatory gastroesophageal polyps

Submucosal mesenchymal tumors
(GIST and inflammatory fibroid polyp)
may present as polyps

Submucosal gland tumors (adenomas)
presenting as polyps



Esophageal squamous papilloma (ESP)

Benign polyp with a **papillary growth pattern** (finger-like processes with a squamous surface epithelium covering a fibrovascular core)

Solitary or multiple

Size can range from **2 to 20 mm**

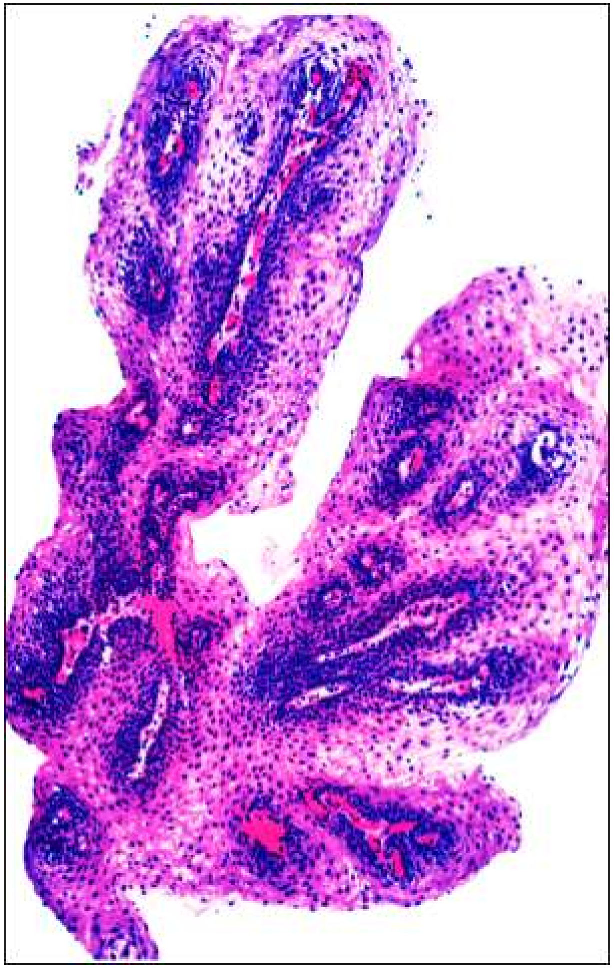
Location

Upper esophagus	30%
Middle esophagus	40%
Lower esophagus	20%
Near or at the *Z*-line	10%

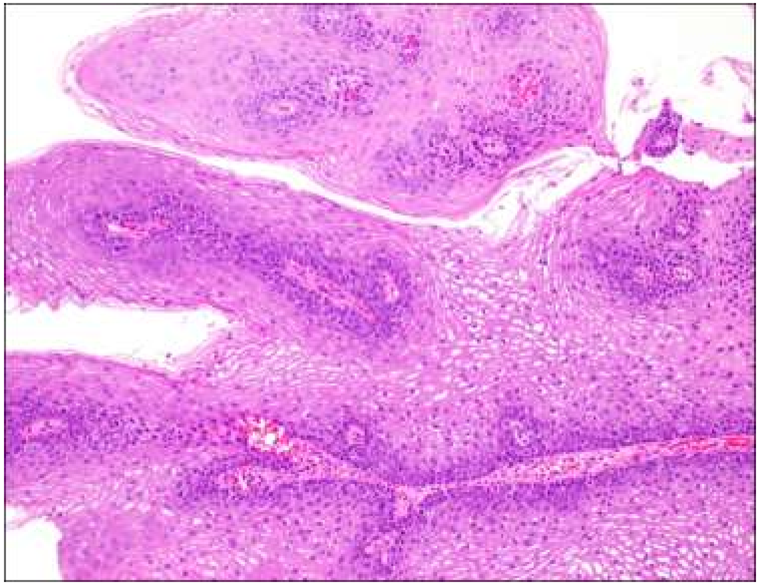
Causes

- **HPV** infection
- **Genodermatosis** (Epidermodysplasia verruciformis)
- **Chronic mucosal irritation**

Non-specific symptom profile



Esophageal squamous papilloma (ESP)



Fibrovascular (fibroepithelial) polyp of the esophagus

Synonyms include fibroepithelial polyp, fibroma, fibrolipoma, pedunculated lipoma

Uncommon benign tumor of the esophagus

80% arise in the **proximal esophagus**

Can present as **intraluminal** growths or **intramural** growth or both

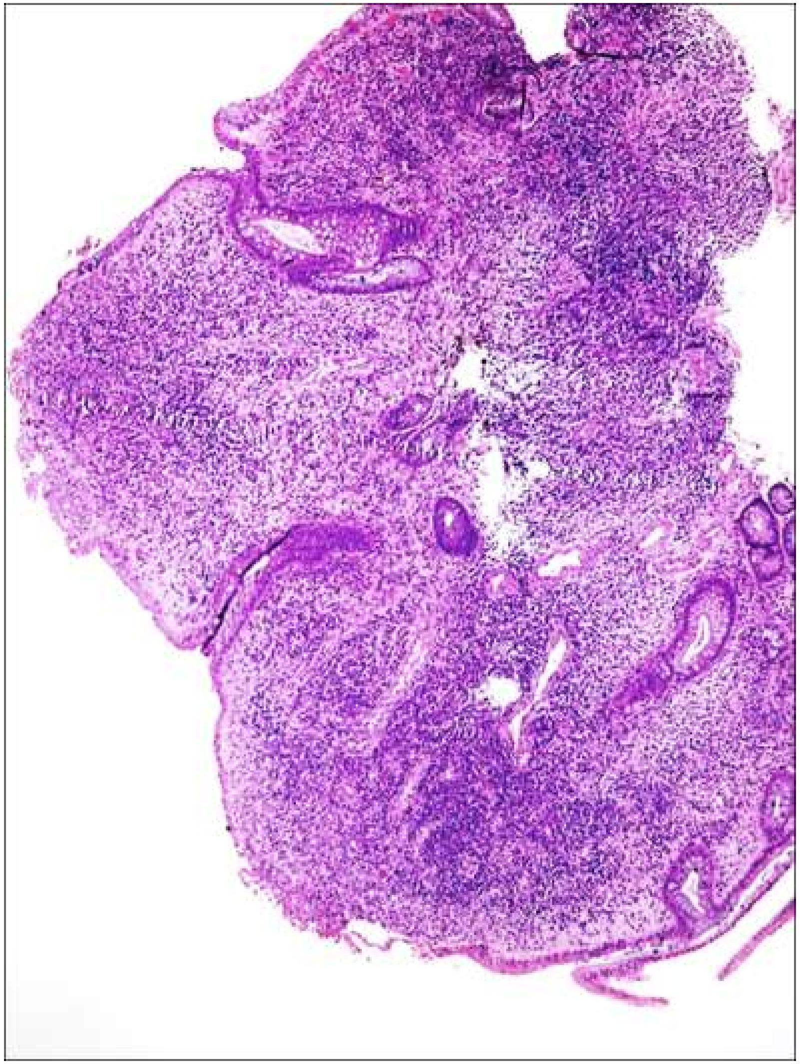
Inflammatory gastroesophageal junction polyps

Inflamed and ulcerated polypoid mucosa

Inflammatory **granulation tissue**

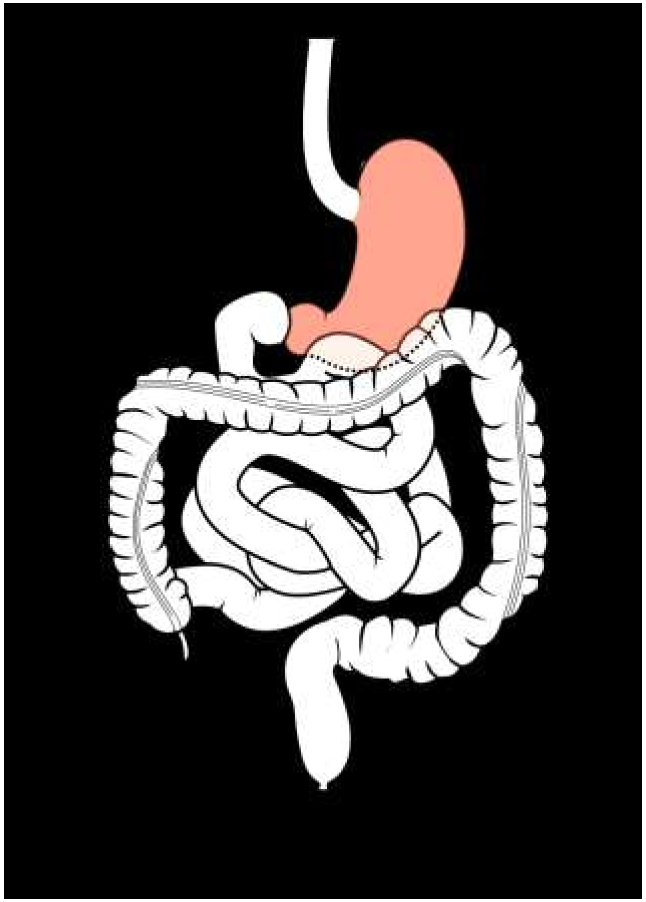
Associated with **Barrett esophagus** (ultra short BE), reflux esophagitis and hiatus hernia

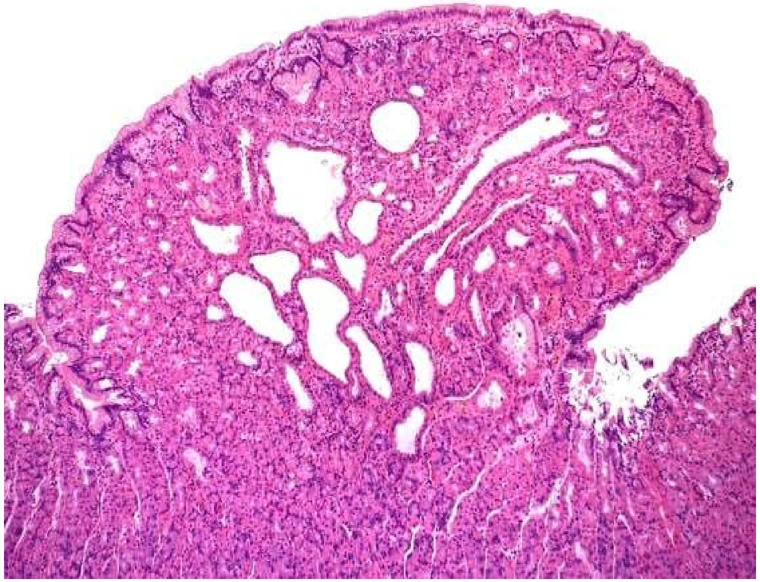
Similar polyps have been reported in the **stomach, small bowel and colon**



Polyps of the stomach

Non-neoplastic polyps (very common)	**90%**
Fundic gland polyp 70%	
Gastric hyperplastic polyp 20%	
Adenomatous polyps (uncommon)	**<5%**
Intestinal (conventional) type	
Foveolar type	
Pyloric gland	
Oxyntic gland	
Other polypoid lesions	**5%**





Fundic Gland Polyps (FGP)

Account for **70%** of gastric polyps (found in up to 10% of patients undergoing gastroscopy)

Isolated, sporadic lesions of little clinical significance

Fundic gland polyps and polyposis have been described

- Following **drug (PPI) therapy** for gastric acid suppression

- **Heritable syndromes** such as familial adenomatous polyposis **(FAP)**

- Gastric adenocarcinoma and proximal polyposis syndrome **(GAPPS)**

Gastric hyperplastic polyp

Account for **20%** of gastric polyps

Most occur at the **junction of pyloric and corpus mucosa**

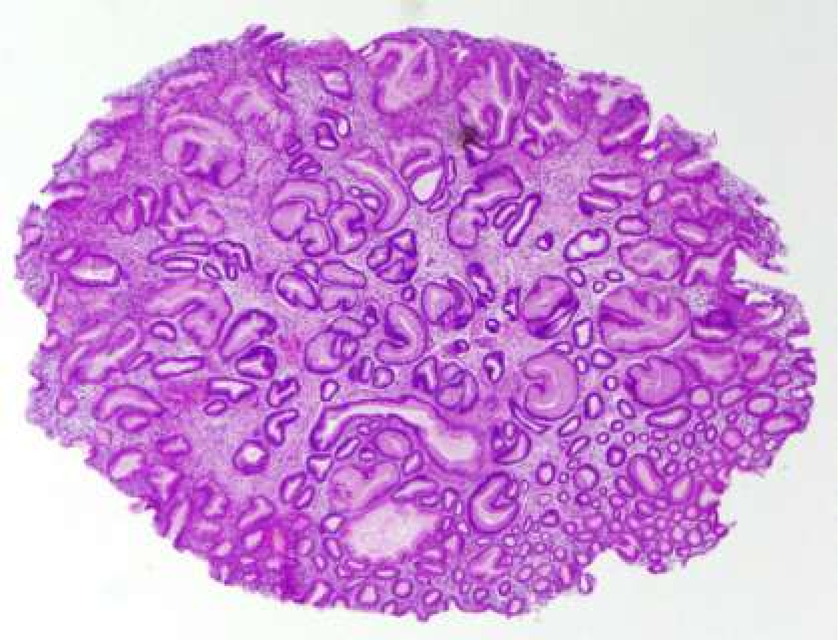
May be **solitary or multiple**

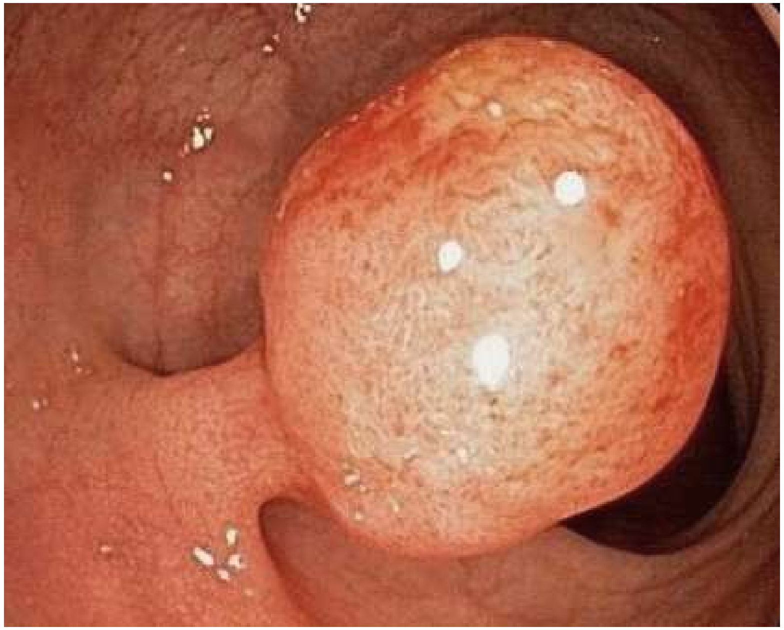
Exaggerated regenerative response to mucosal damage

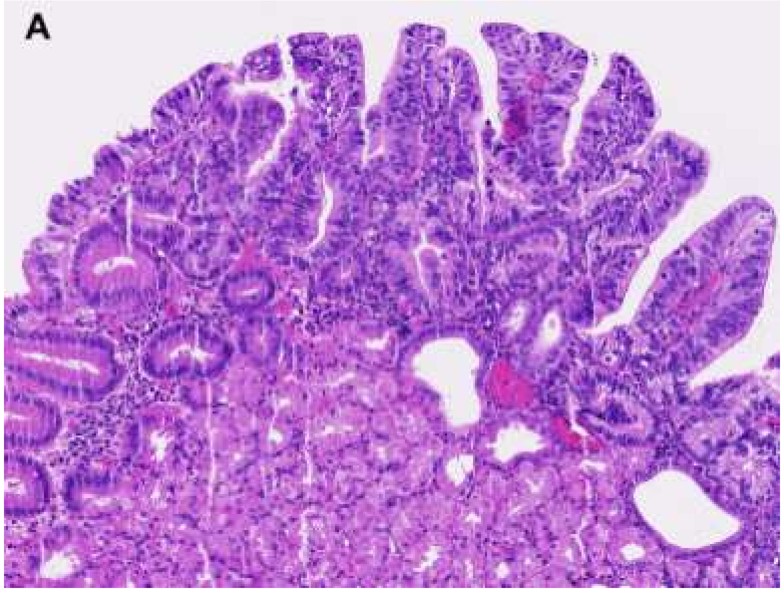
Similar to other **inflammatory polyps** of the GI

Dysplasia is rare in these polyps

Low **risk** of malignancy (large polyps)







Adenomatous polyps

Neoplastic polyps with dysplastic epithelium

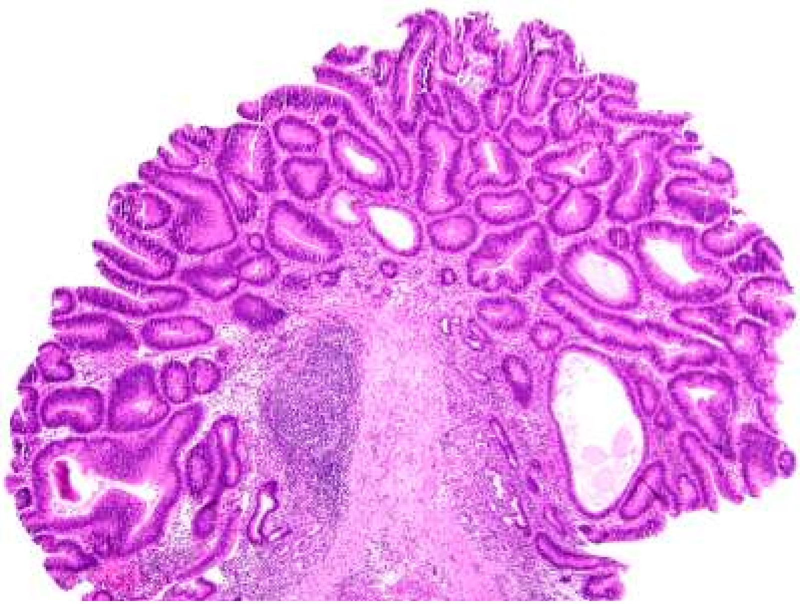
Uncommon (<5% of gastric polyps)

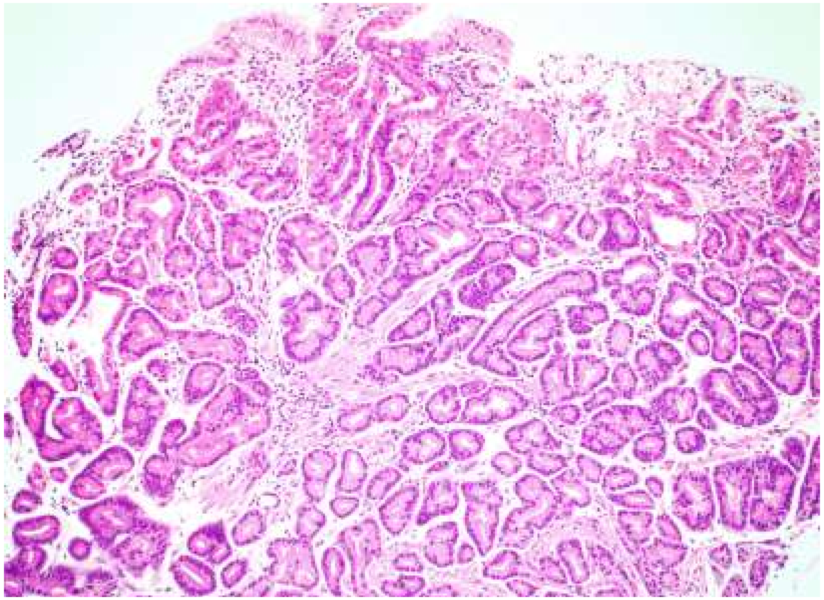
Intestinal, foveolar, pyloric gland or oxyntic gland histology

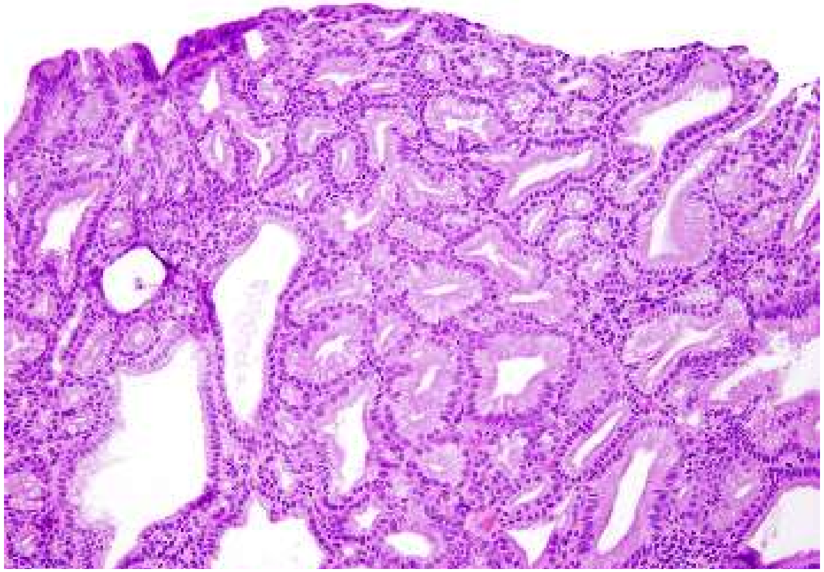
Risk of progression to cancer is high in **large (>2cm) flat adenomas of intestinal type**

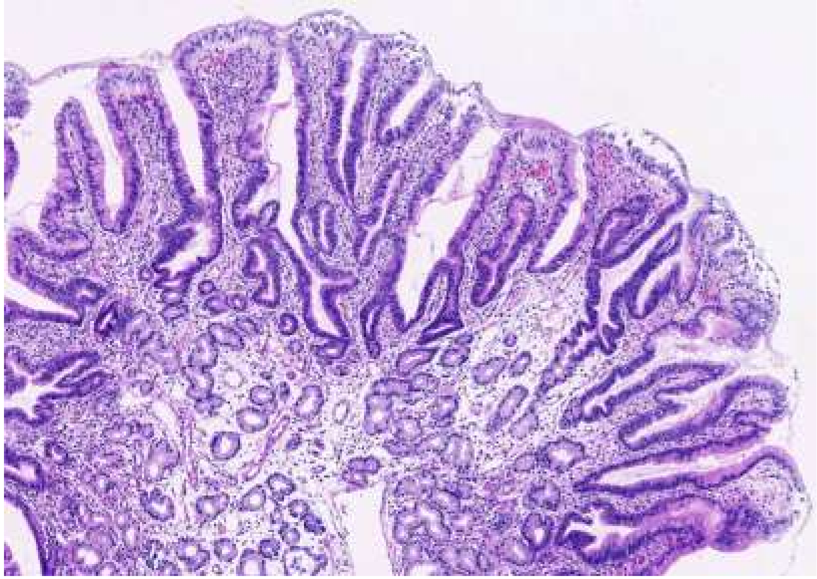
Risk of **coexistent carcinoma** in the stomach is ~10%

Should be **completely removed** and the remainder of the stomach be carefully assessed for additional lesions


Intestinal type adenoma


Oxyntic gland adenoma


Pyloric gland adenoma


Foveolar type adenoma

Other polypoid lesions of the stomach

- Inflammatory fibroid polyps
- Inflammatory myofibroblastic tumor
- Pancreatic heterotopia
- Polypoid tumors (carcinomas, NETs, GISTs, etc)
- Polypoid mucosal prolapse/mucosal prolapse polyp

Polyposis syndromes

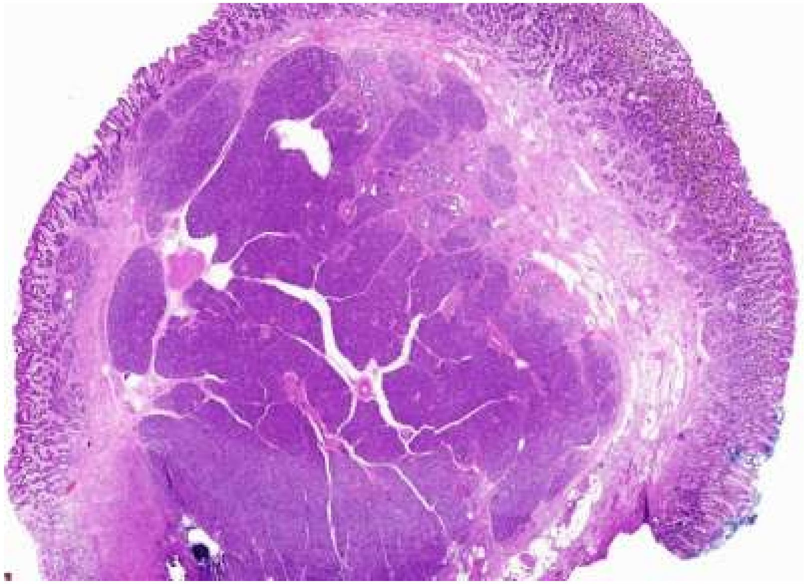
- Familial adenomatous polyposis
- Peutz-Jeghers Syndrome
- Juvenile Polyposis Syndrome
- Cowden Syndrome
- Cronkhite-Canada Syndrome
- Other syndromes

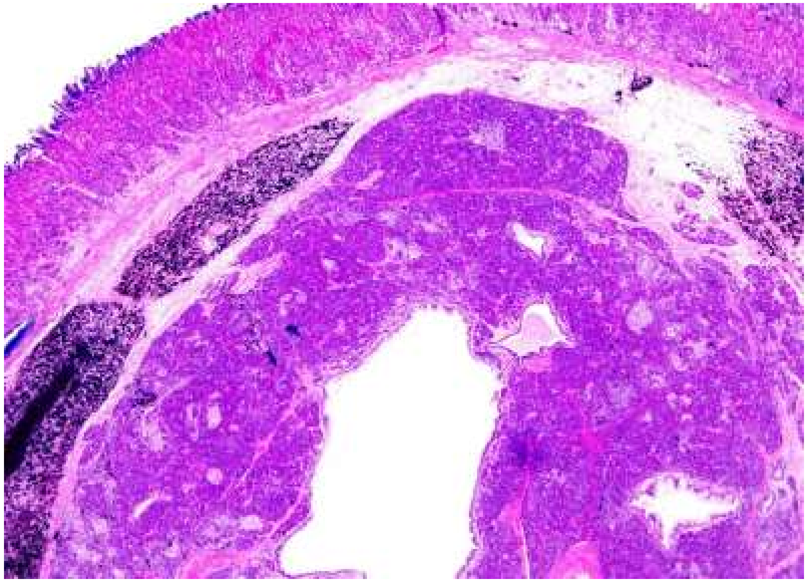
Heterotopic pancreas

Benign pancreatic tissue, anatomically **separate from the main pancreas** with **no vascular or ductal connection to the pancreas**

Composed of a variable mixture of pancreatic **acini, ducts and islets**

Most common in **stomach** but may occur throughout GI tract





Heterotopic pancreas

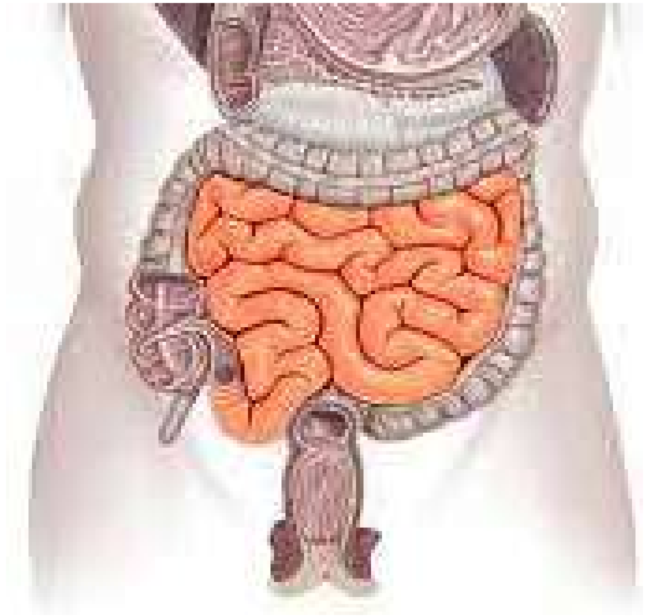
May be **asymptomatic** or depending on **size and location**, may present with symptoms such as abdominal **pain, GI bleed or obstruction**

May develop the same diseases as the main pancreatic gland **(endocrine and non-endocrine neoplasms)**

Polyps of the small intestine and ampulla

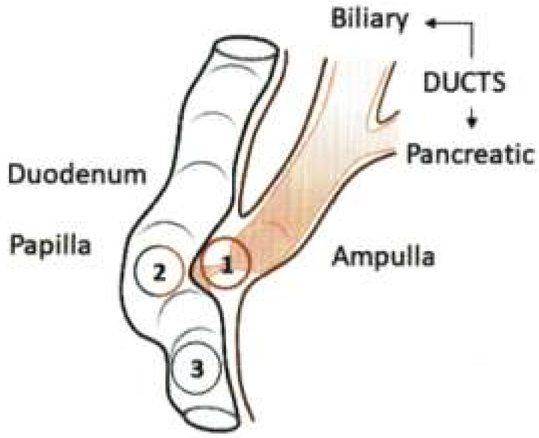
Epithelial (adenomatous) polyps

- Ampullary adenomas
  - Intestinal type
  - Pancreatobiliary type
- Non-ampullary adenomas
  - Intestinal type
  - Pyloric gland type



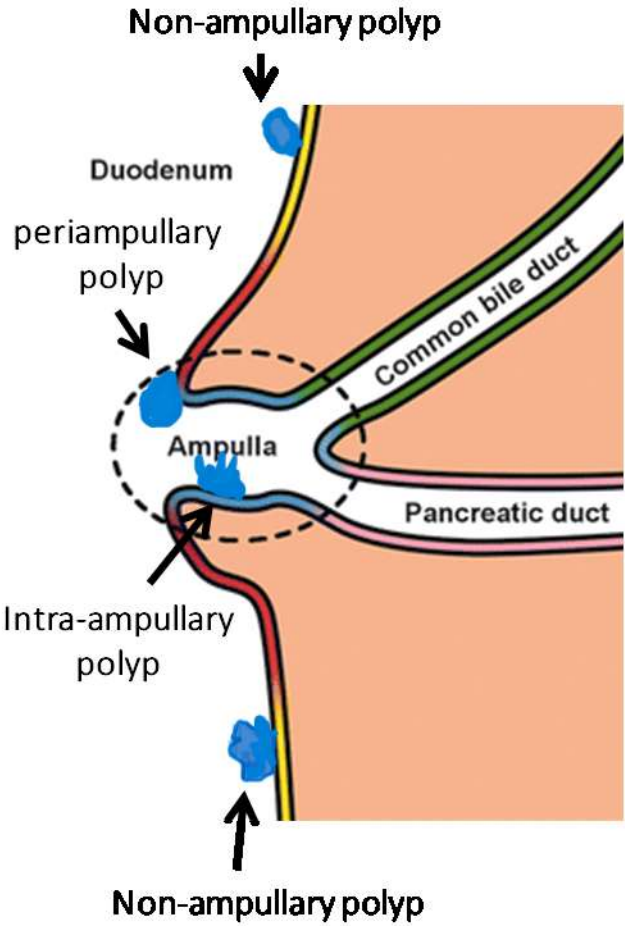
Mesenchymal polyps

- Inflammatory fibroid tumor
- Inflammatory myofibroblastic tumor
- GIST
- Other



1 Ampullary duct
2 Periampullary (duodenal) area
3 Extra-ampullary (duodenal) area

Polyposis syndromes


Non-ampullary polyp
Duodenum
periampullary polyp
Common bile duct
Ampulla
Pancreatic duct
Intra-ampullary polyp
Non-ampullary polyp

Tumors and polyps of the small intestine

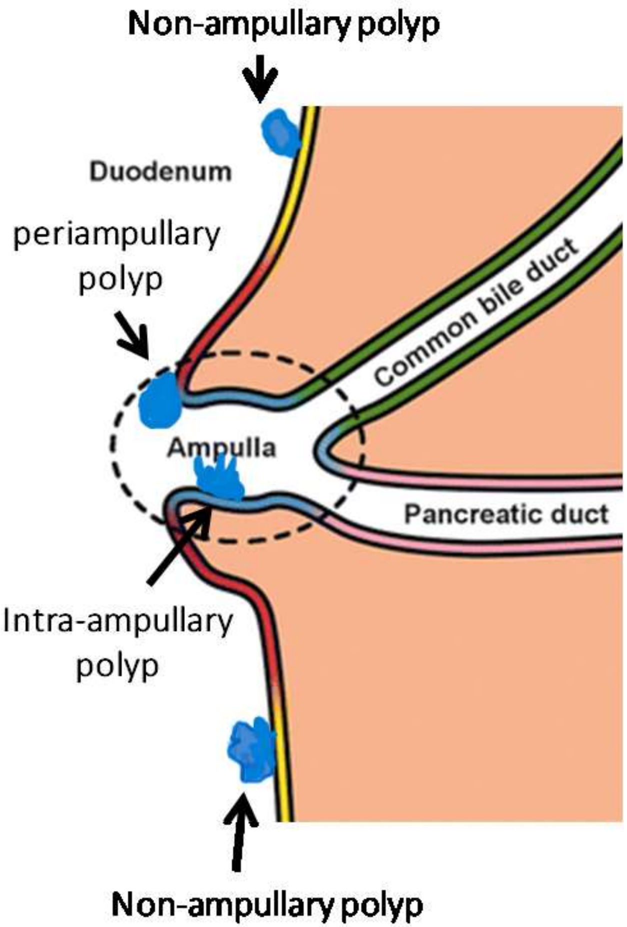
<10% of all GI tract neoplasms occur in the small bowel despite the fact that the mucosal surface of the **small bowel covers >90% of the entire GI system**

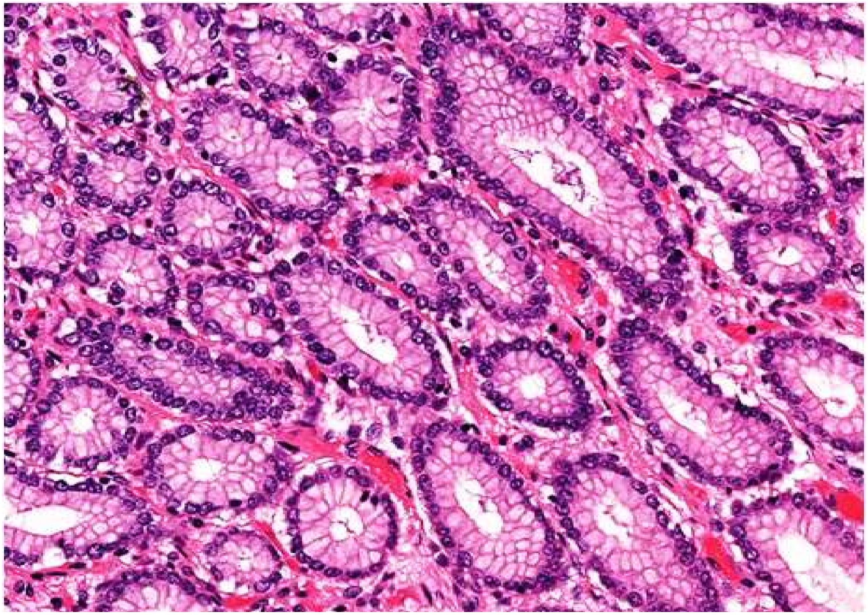
Prevalence of polyps and tumors decreases progressively from the **duodenum (55–75%), to the jejunum (15%-25%), to the ileum (10%–15%)**

Duodenal polyps can be ampullary or non-ampullary

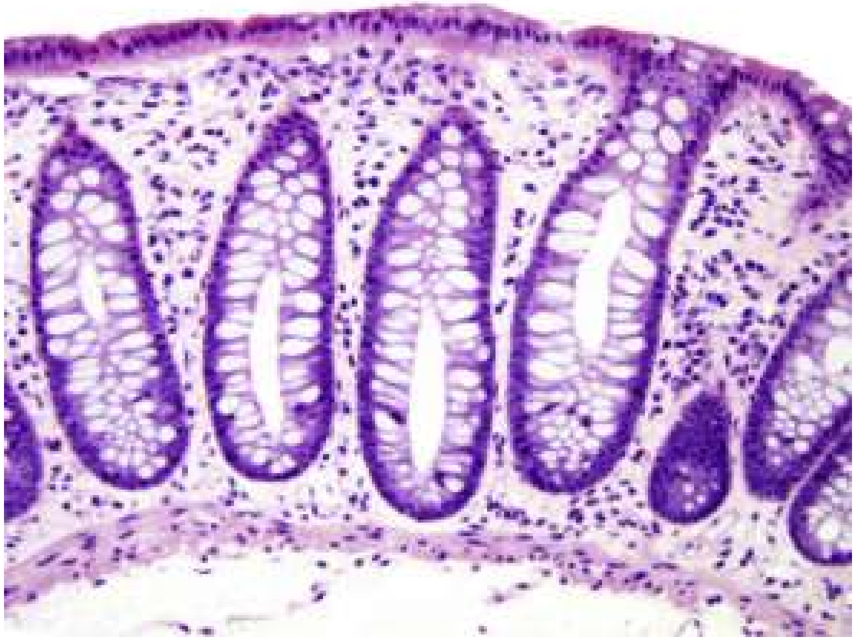
Ampullary polyps can be **intra-ampullary** in the ampullary channel or **periampullary** on the duodenal surface of the ampulla

Ampullary polyps can have intestinal or pancreatobiliary epithelium whereas **small bowel polyps display intestinal or pyloric** histology

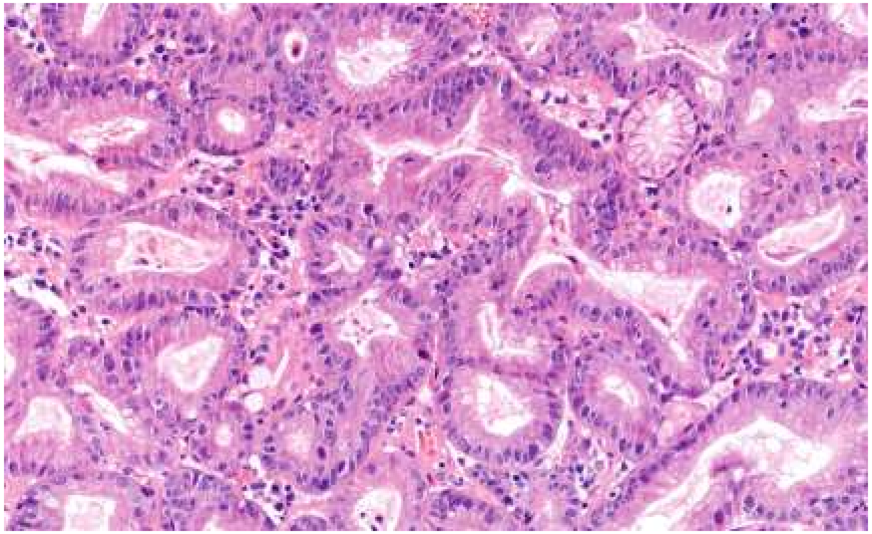




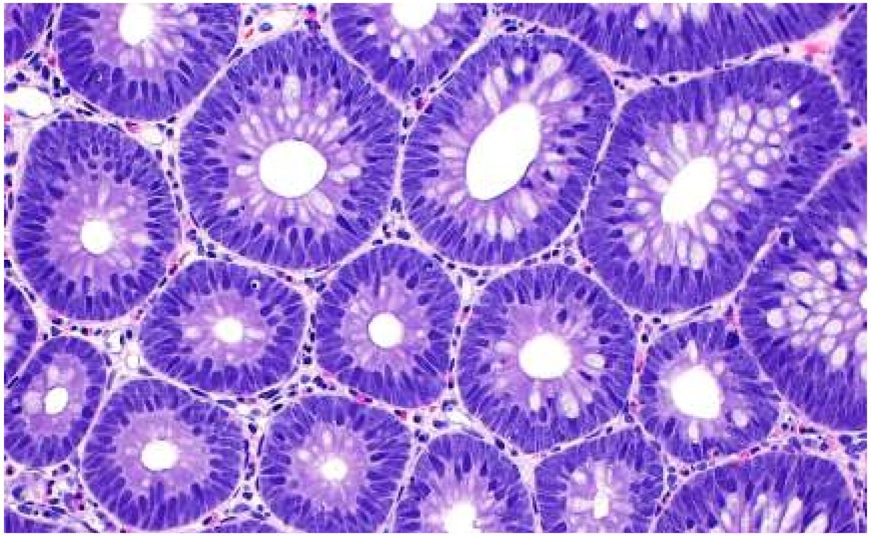
Normal pyloric epithelium



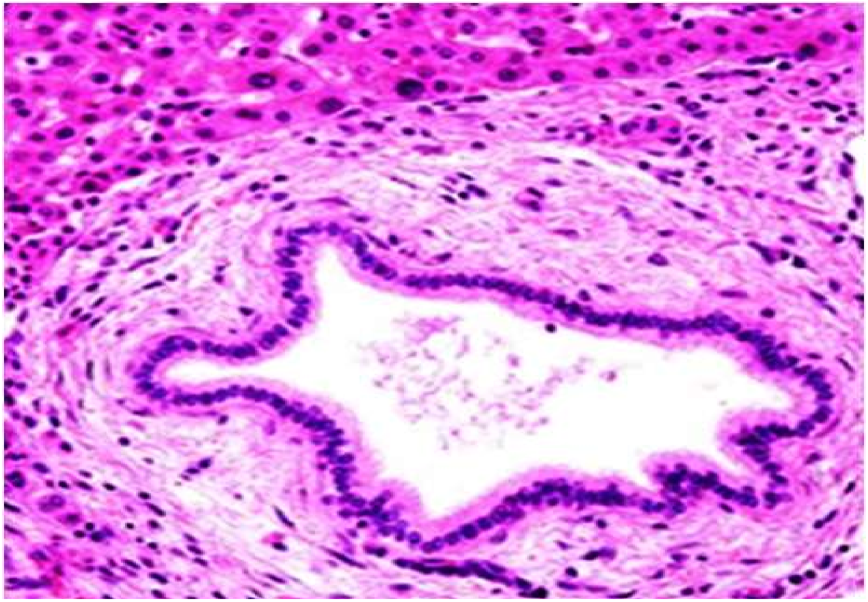
Normal colorectal epithelium



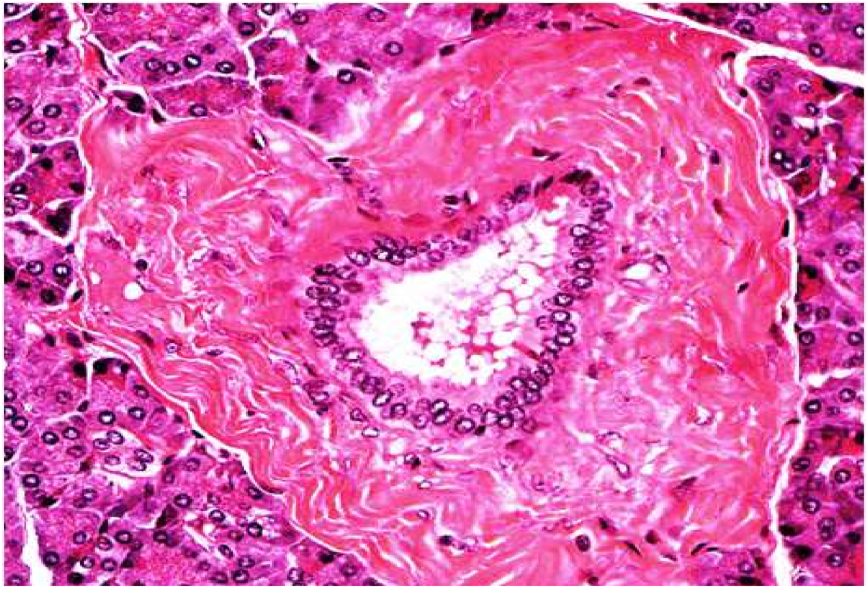
Dysplastic pyloric epithelium



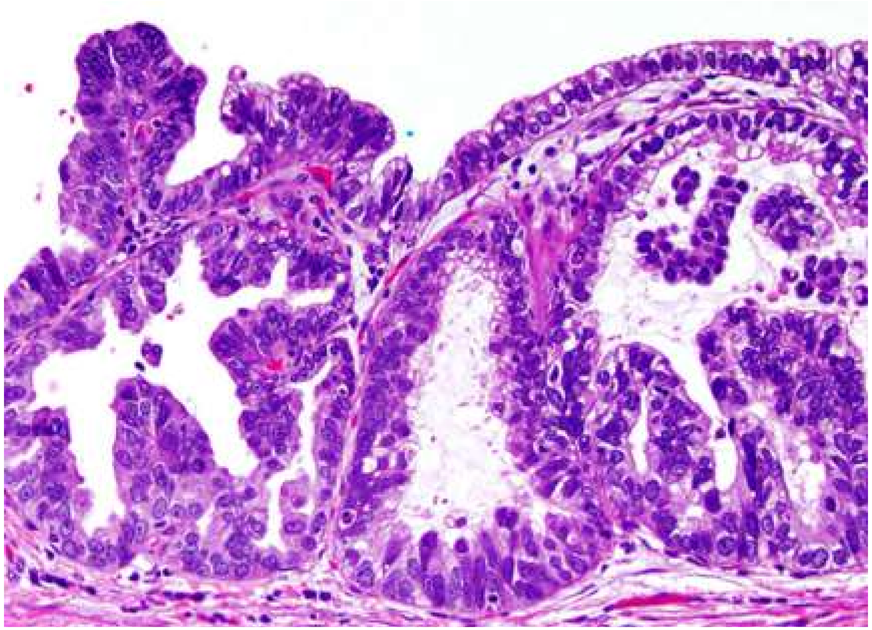
Dysplastic intestinal epithelium



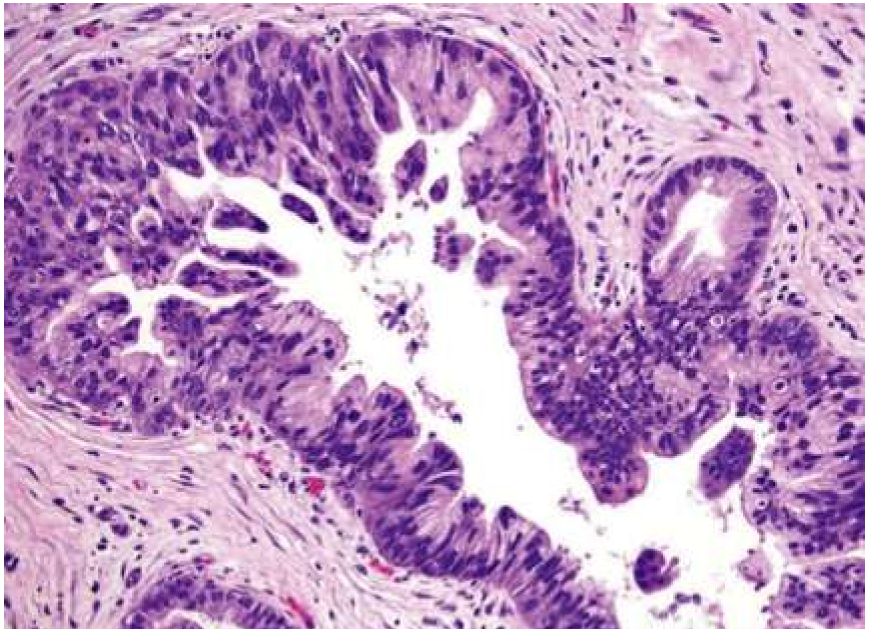
Normal bile duct epithelium



Normal pancreatic duct epithelium

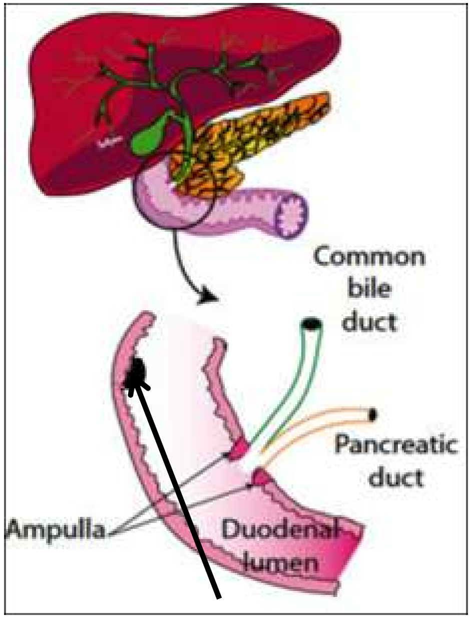


Dysplastic bile duct epithelium

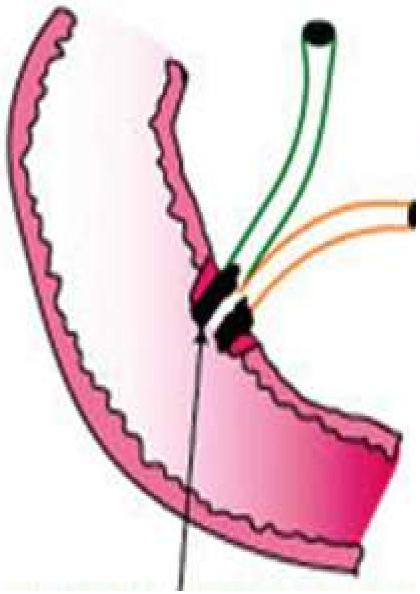


Dysplastic pancreatic duct epithelium

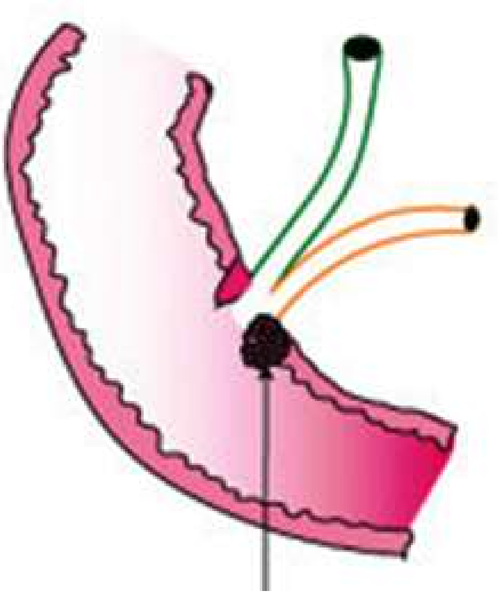
Small bowel polyps and epithelial neoplasms	
Ampullary	Non-ampullary
Intra-ampullary Periampullary	Duodenum Jejunum Ileum



Non-ampullary



Intra-ampullary



Periampullary

Ampullary

<table>
<tr><th colspan="2">Ampullary adenomas</th></tr>
<tr><th>Intra-ampullary adenomas</th><th>Periampullary adenomas</th></tr>
<tr><td>Papillary-tubular neoplasm</td><td>Tubular adenoma</td></tr>
<tr><td>Pancreatobiliary type epithelium</td><td>Intestinal type epithelium</td></tr>
<tr><td>Occurs within the intra-ampullary channel</td><td>Occur on the duodenal surface of the ampulla</td></tr>
<tr><td colspan="2">Cause biliary obstruction (jaundice, cholangitis or pancreatitis)</td></tr>
<tr><td>Difficult to assess and biopsy</td><td>Easier to assess and biopsy</td></tr>
<tr><td colspan="2">Complete removal though curative may be difficult to achieve endoscopically (small lesions are amenable to endoscopic resection but larger adenomas may require pancreatoduodenectomy)</td></tr>
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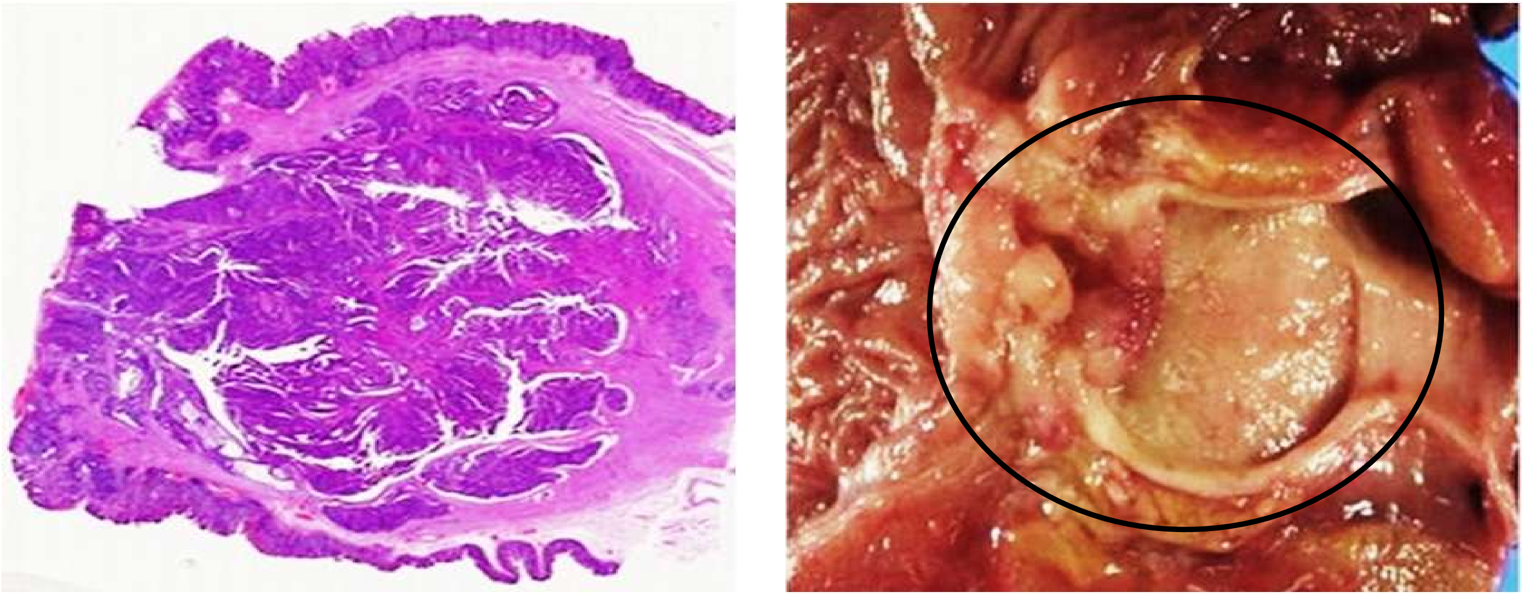
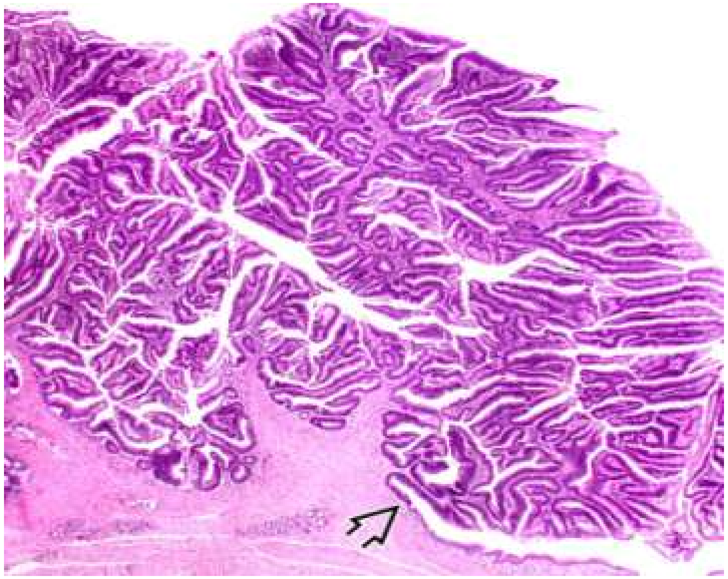
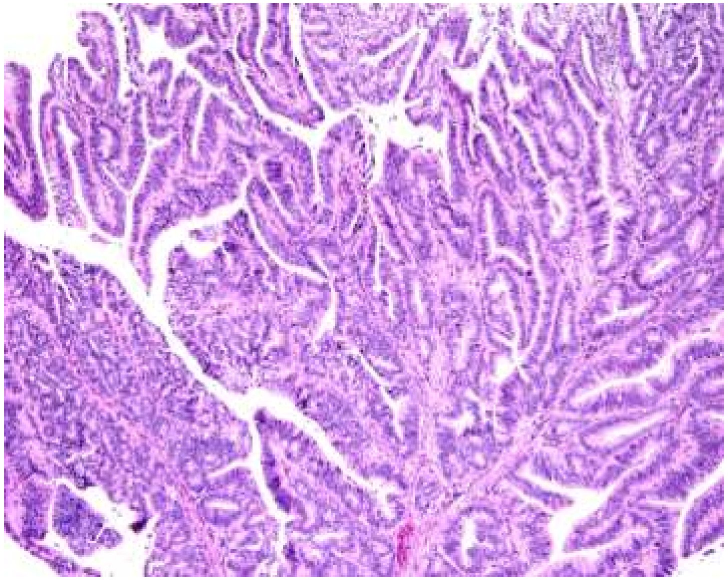


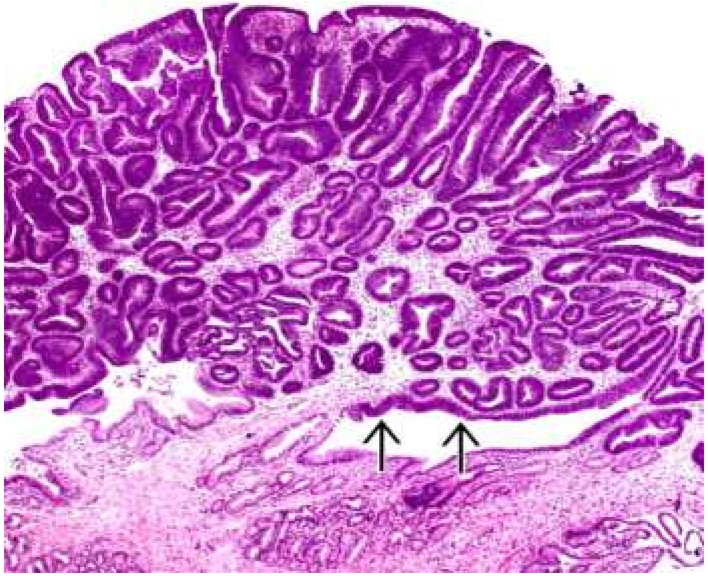
Intra-ampullary adenoma

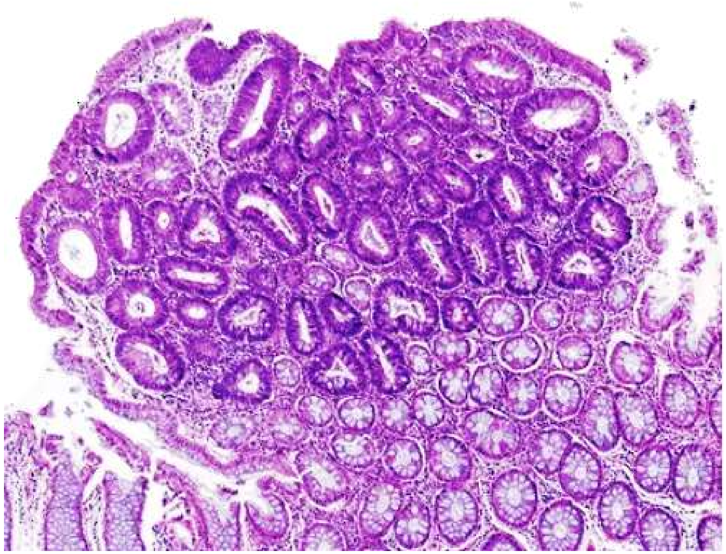
Peri-ampullary adenoma





Pancreatobiliary histology





Intestinal histology

Non-ampullary small intestinal adenomas

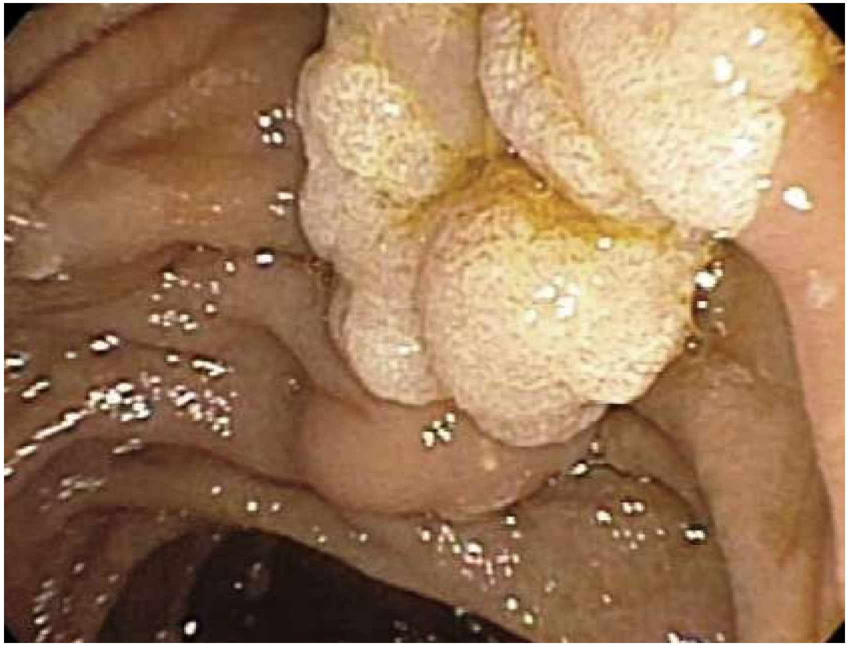
More common in the **proximal small bowel**

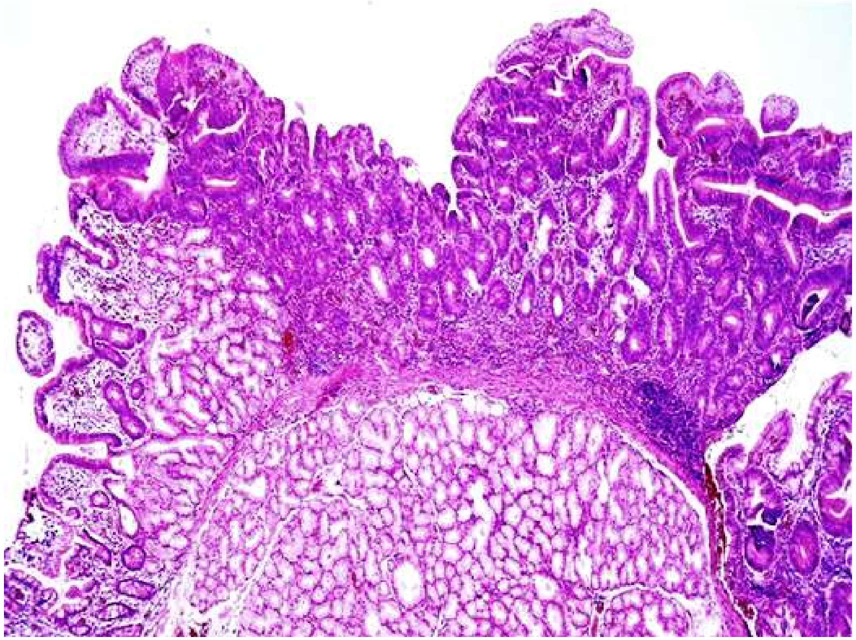
Most occur in proximal duodenum

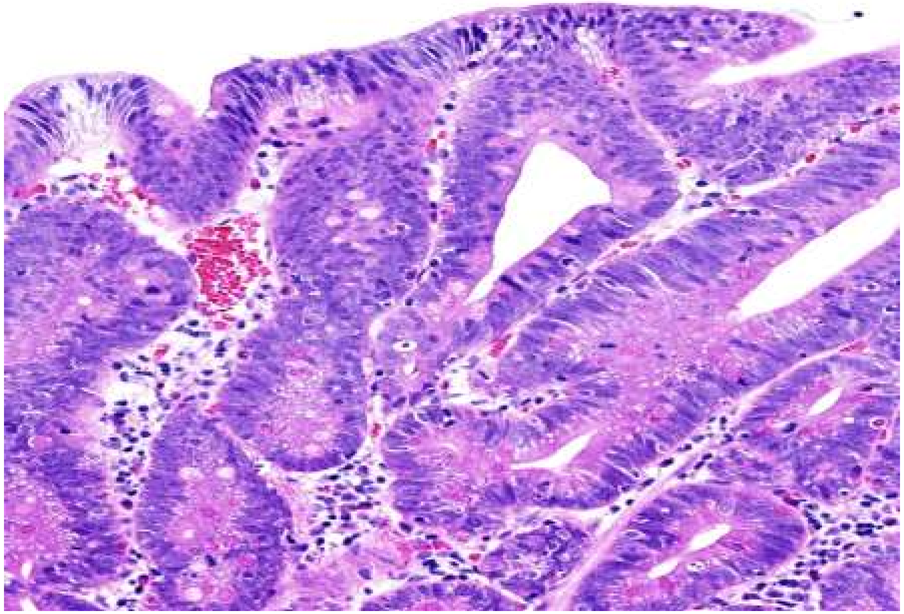
Generally **asymptomatic** and may go unnoticed until carcinoma develops

Risk of developing invasive disease is related to

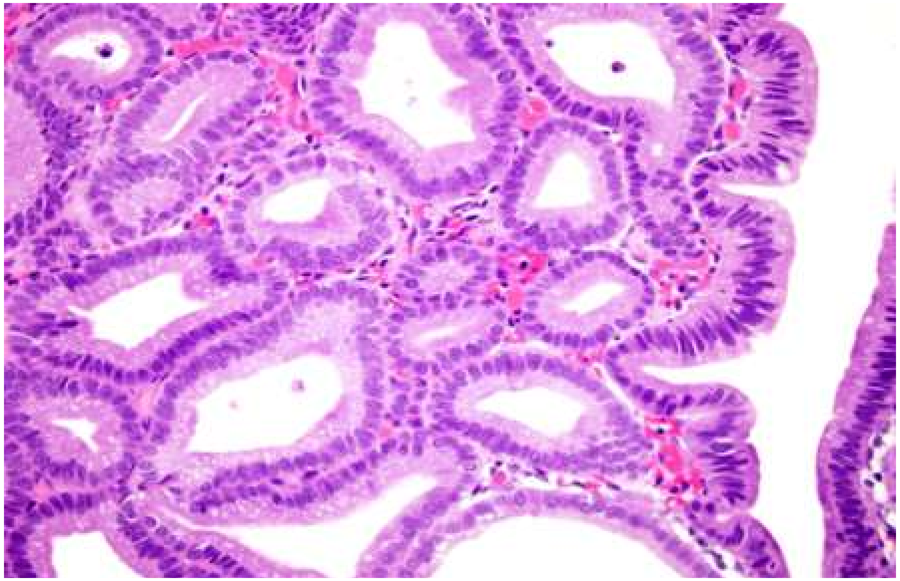
- Size of the adenoma
- Villous component
- High grade dysplasia(HGD)







Intestinal type adenoma



Pyloric gland type adenoma

Non-ampullary small intestinal adenomas

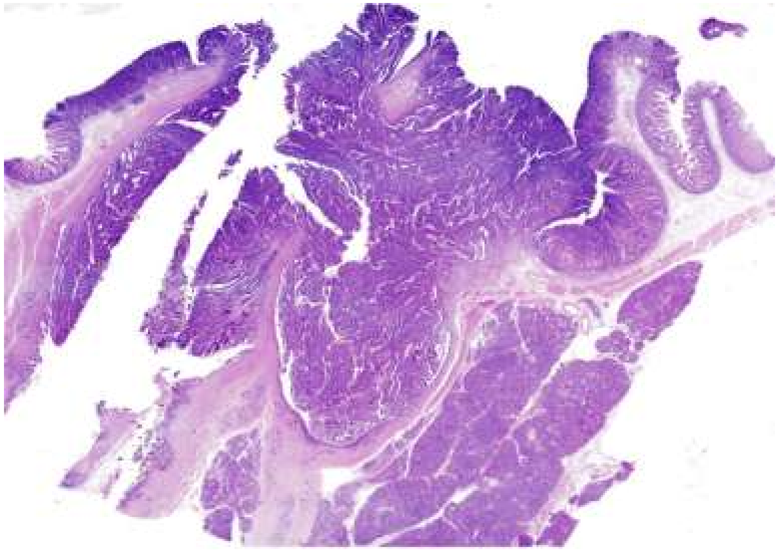
Neoplastic polyps with **dysplastic glandular epithelium**

May show **intestinal-type or pyloric gland** differentiation

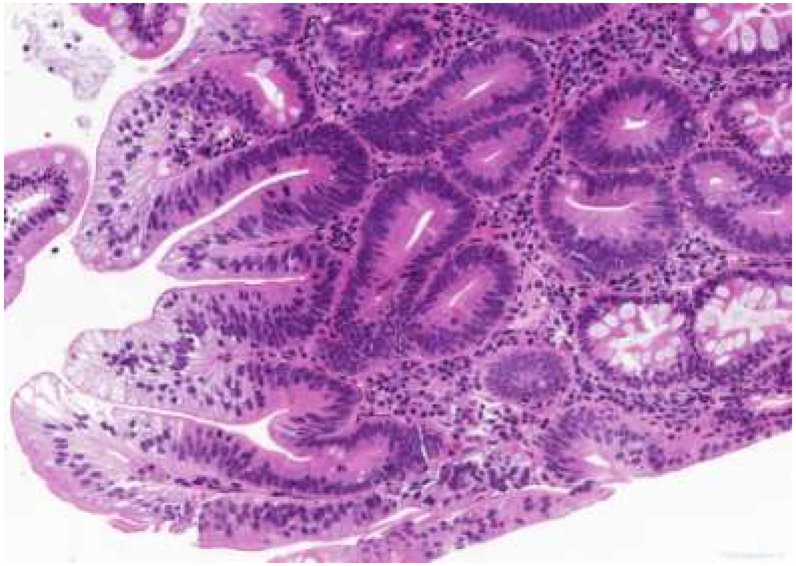
Intestinal-type adenomas develop **anywhere in the small intestine**, with the proximal duodenum close to the ampulla being the most frequent sites

Pyloric gland adenomas are mostly located in the proximal duodenum

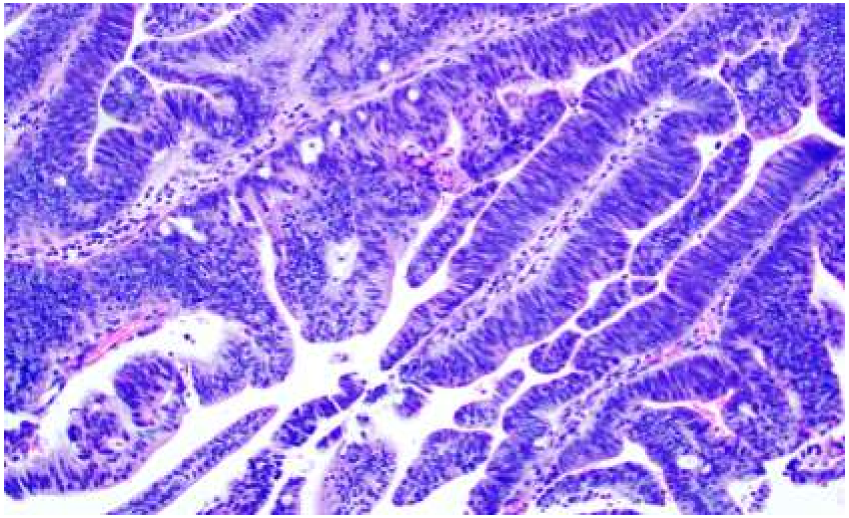
Ampullary adenoma
Pancreatobiliary type



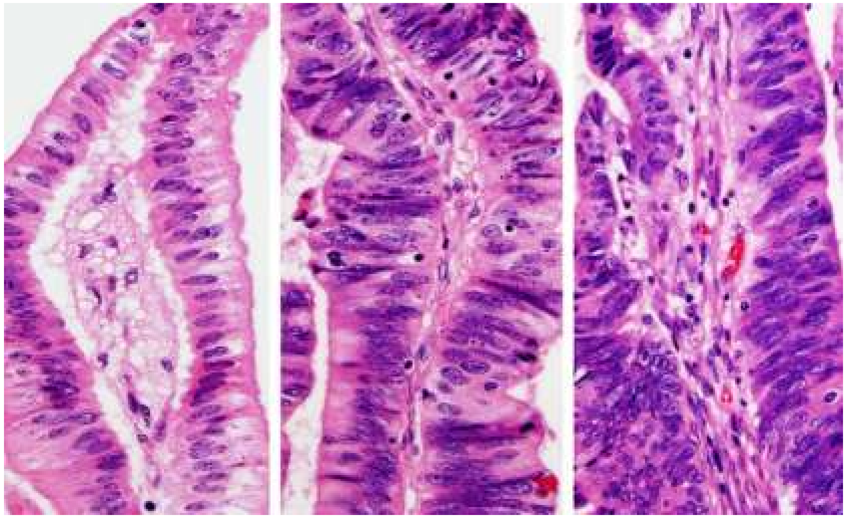
Non-ampullary adenoma
Intestinal type



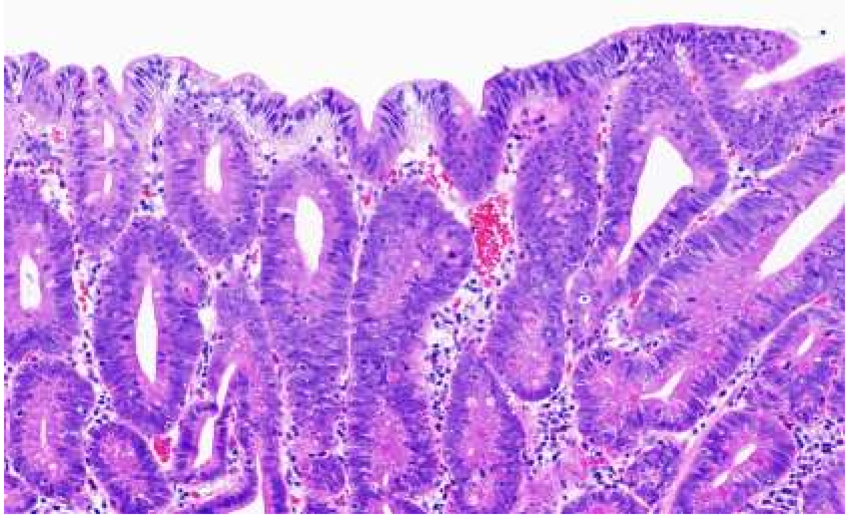
Polyps of the small intestine and ampulla



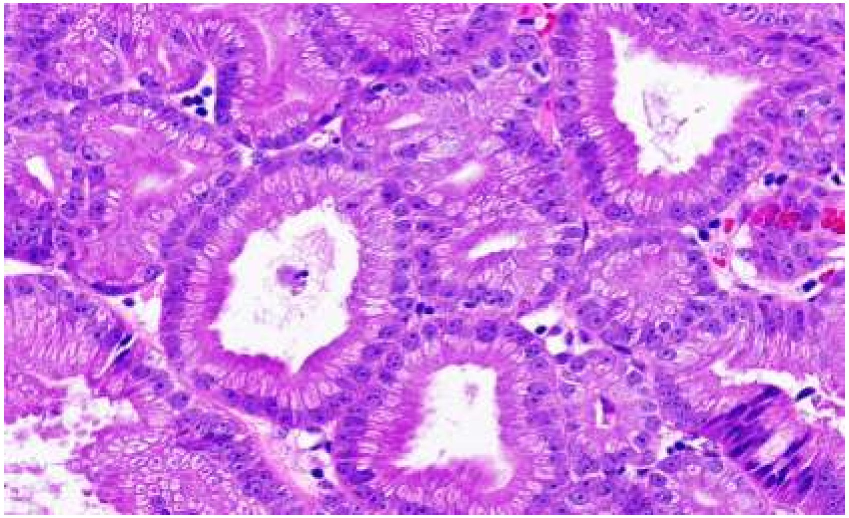
Ampullary adenoma, intestinal type



Ampullary adenoma, pancreatobiliary type



Non-ampullary adenoma, intestinal type

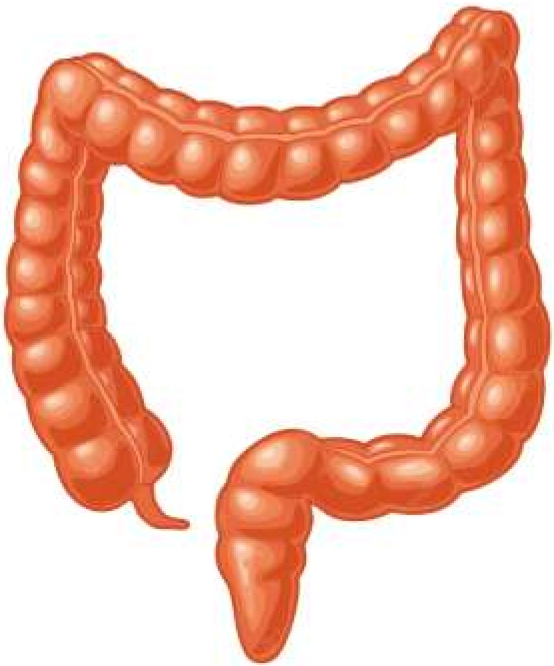


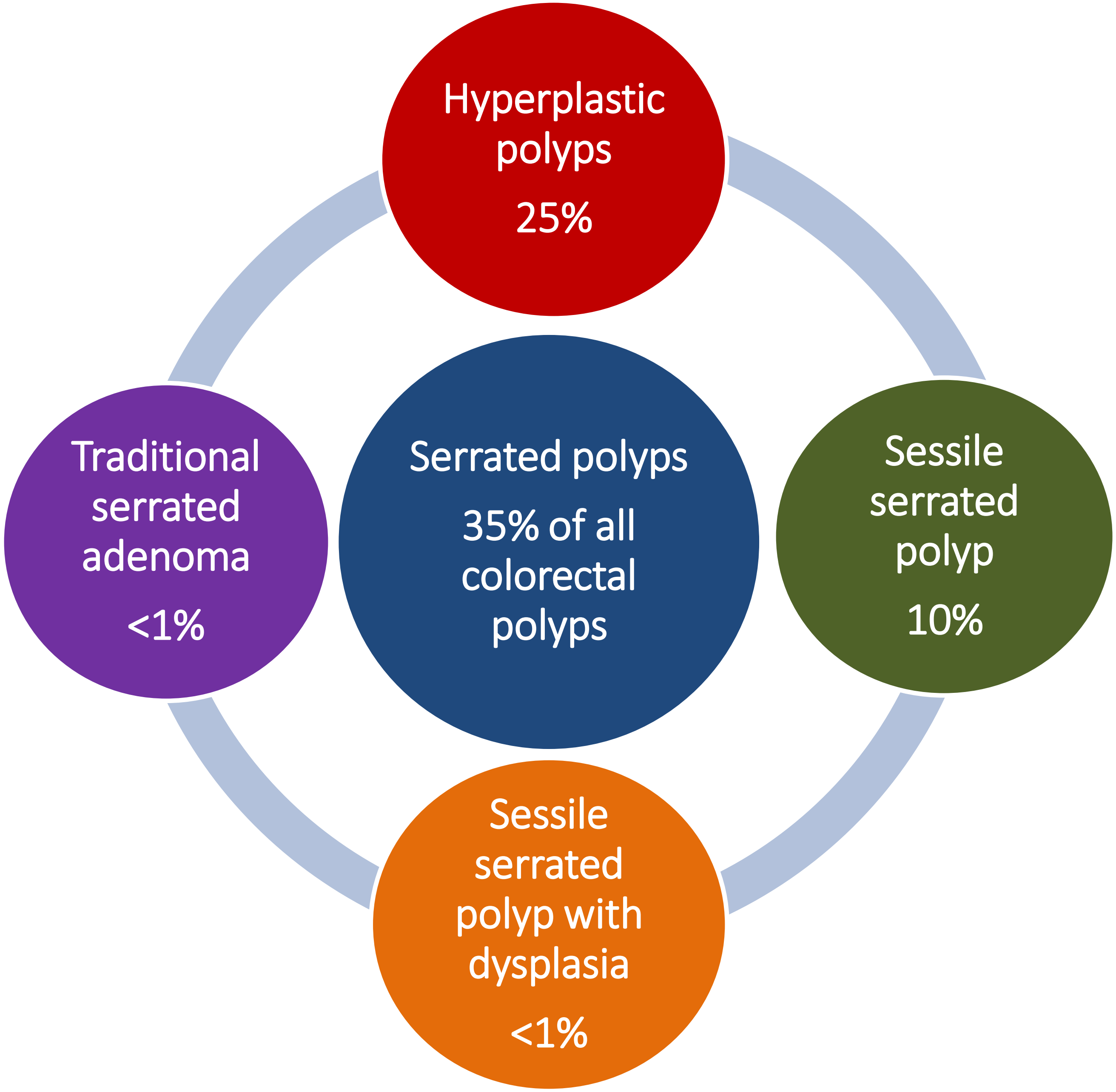
Non-ampullary adenoma, pyloric gland type

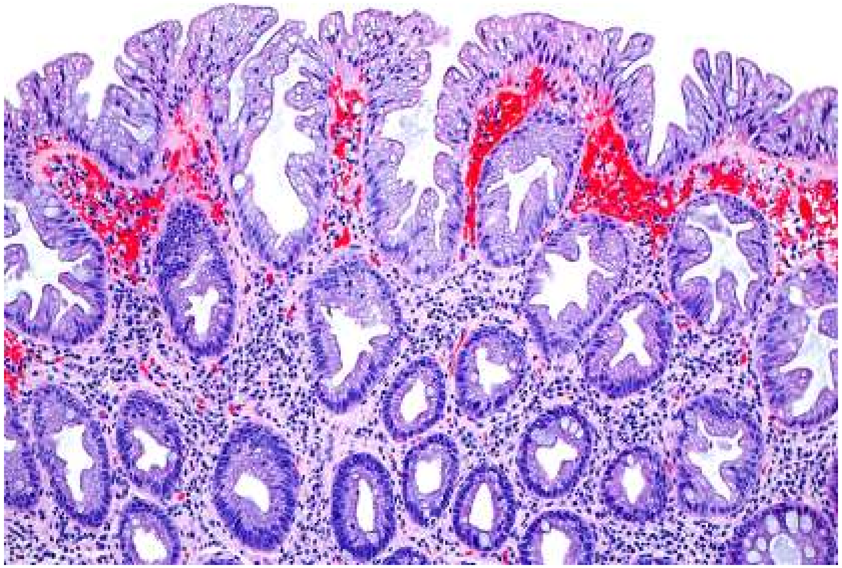
Polyps of the colorectum and appendix

Polyps of the colorectum

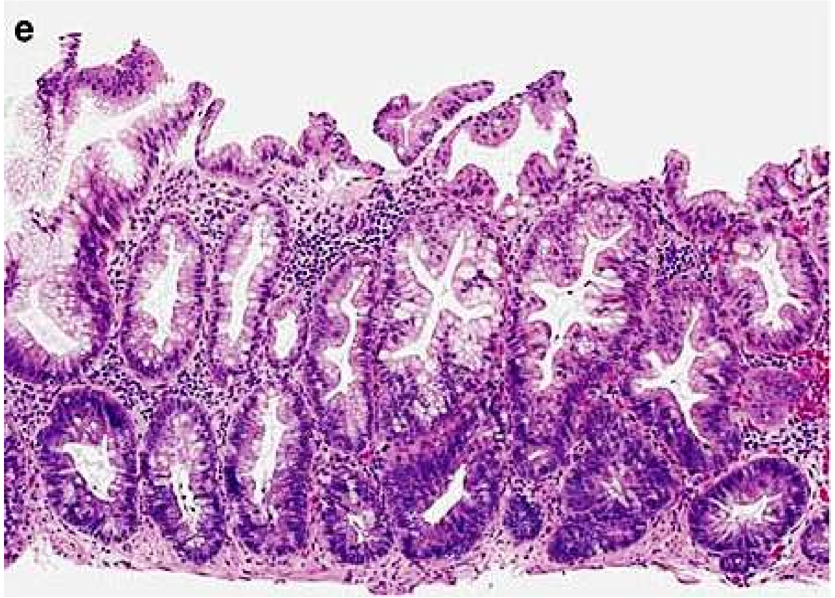
- Serrated polyps 30%
- Adenomatous polyps 65%
- Other types 5%



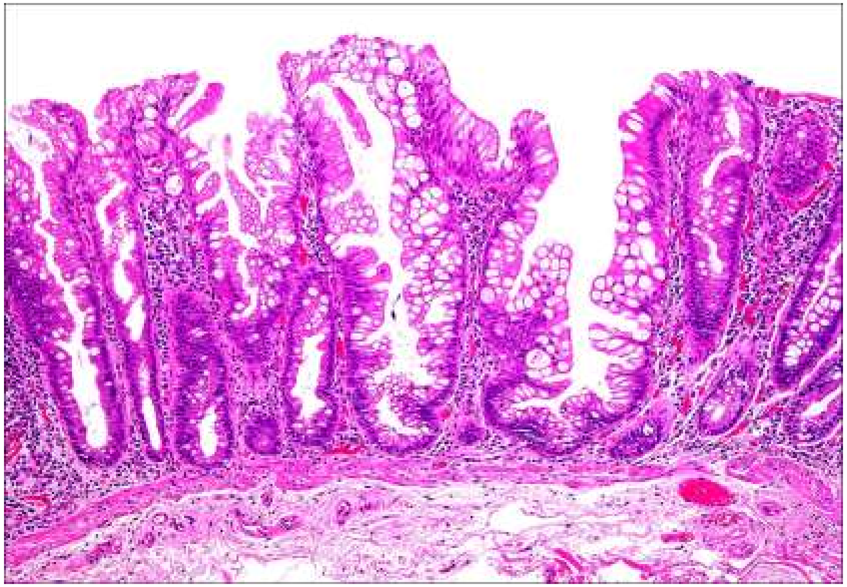

Hyperplastic polyps
25%
Traditional serrated adenoma
<1%
Serrated polyps
35% of all colorectal polyps
Sessile serrated polyp
10%
Sessile serrated polyp with dysplasia
<1%



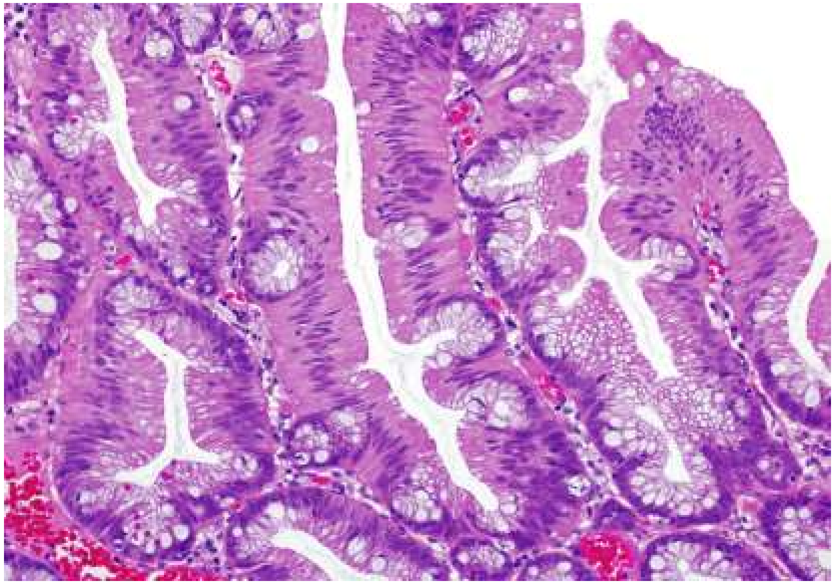
Hyperplastic polyp



Sessile serrated polyp with dysplasia

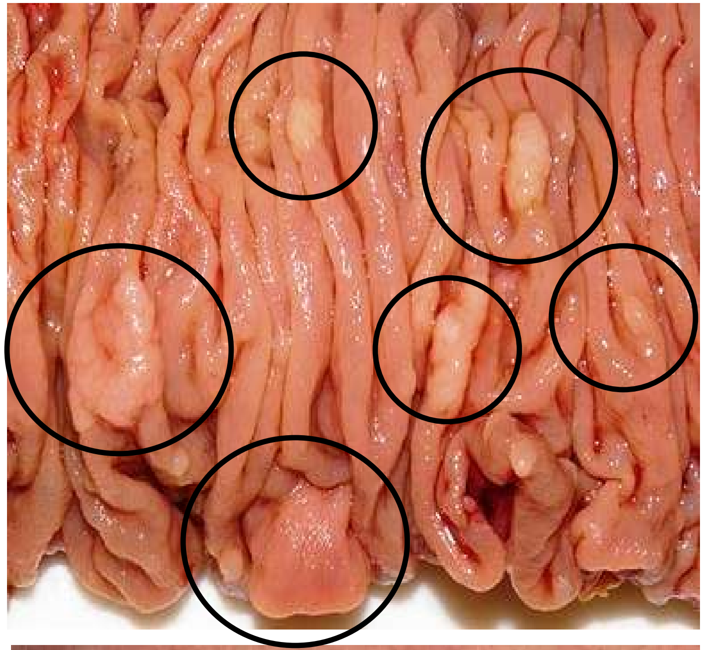


Sessile serrated lesion/polyp



Traditional serrated adenoma

Serrated polyps of the colorectum



Hyperplastic Polyp

Most common serrated colorectal polyps

Usually **small** (<5 mm)

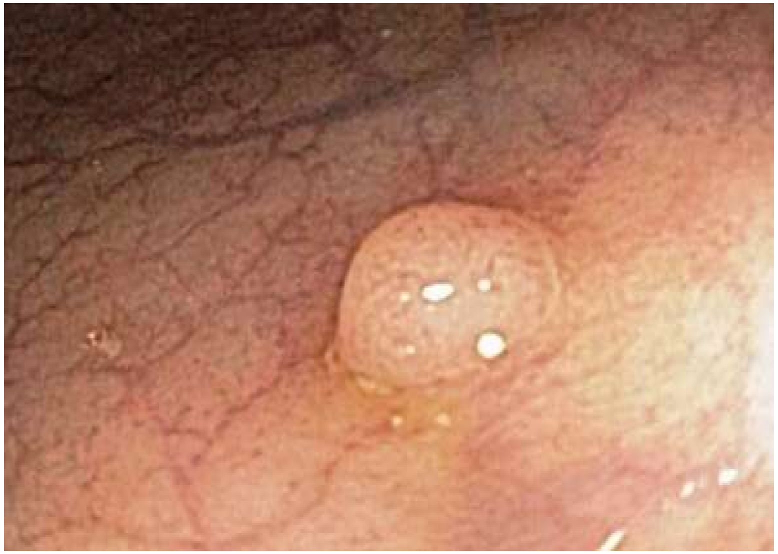
Predilection for the **distal colon and rectum**

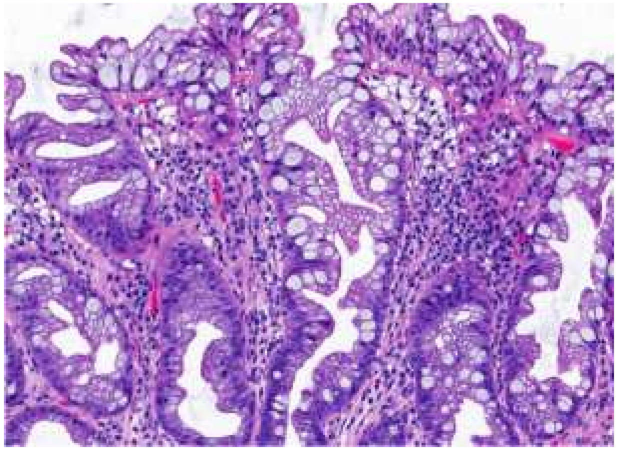
Benign with negligible cancer risk

Pale, dome-shaped sessile nodules of similar color with the background

Microvesicular, goblet cell-rich and mucin poor subtypes recognised

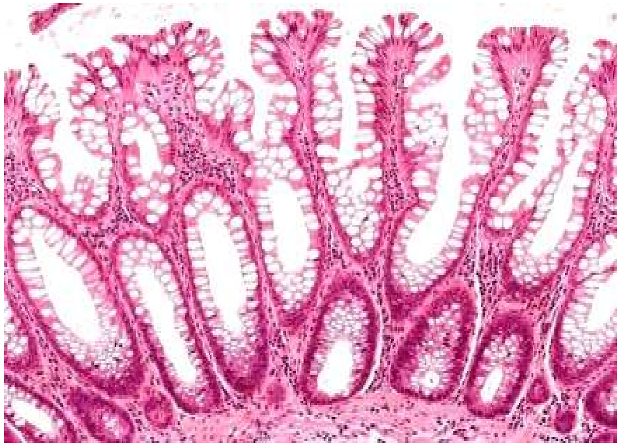
Subclassification is not warranted in clinical practice





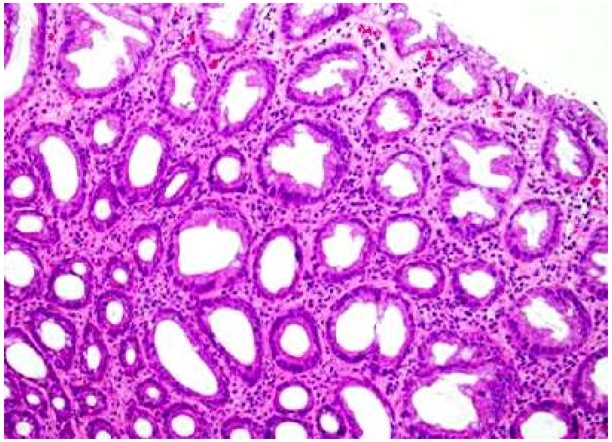
Microvesicular hyperplastic polyp (MVHP)

Multiple mucin droplets in the cytoplasm



Goblet cell–rich hyperplastic polyp (GRHP)

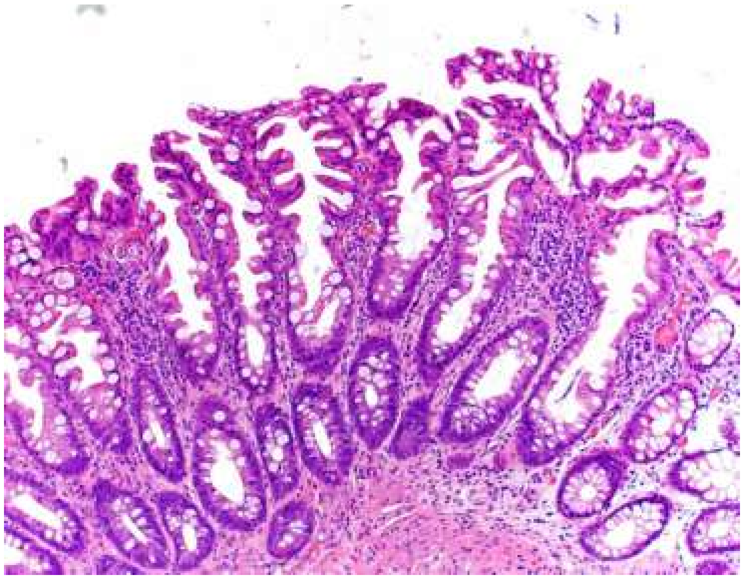
Single mucin droplet in the cytoplasm

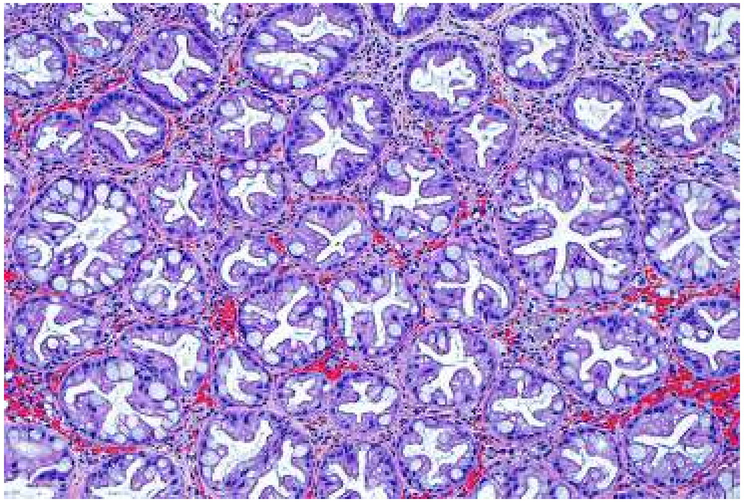


Mucin poor hyperplastic polyp (MPHP)

Very little mucin in the cytoplasm

No longer in use





Hyperplastic polyp

Serrated architecture (saw tooth) appearance, limited to the upper half of the crypts

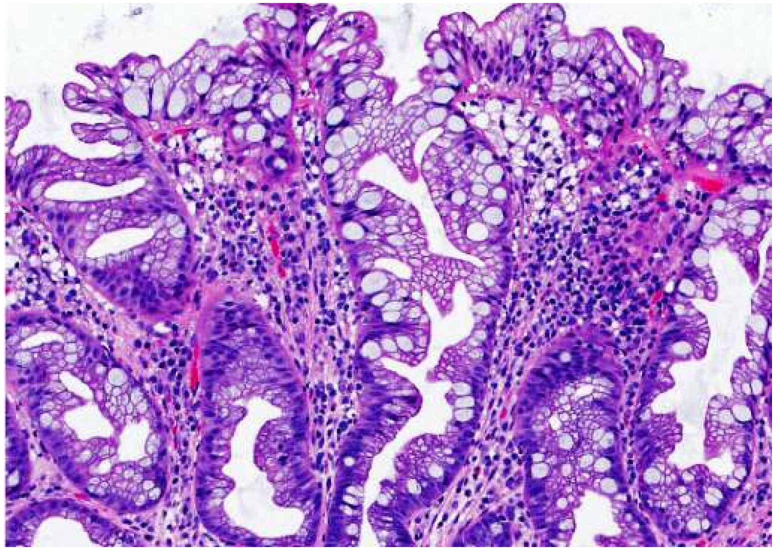
Mild nuclear enlargement, stratification and hyperchromasia in crypt base

NO dilated, branched or horizontally spreading crypts

NO conventional dysplasia

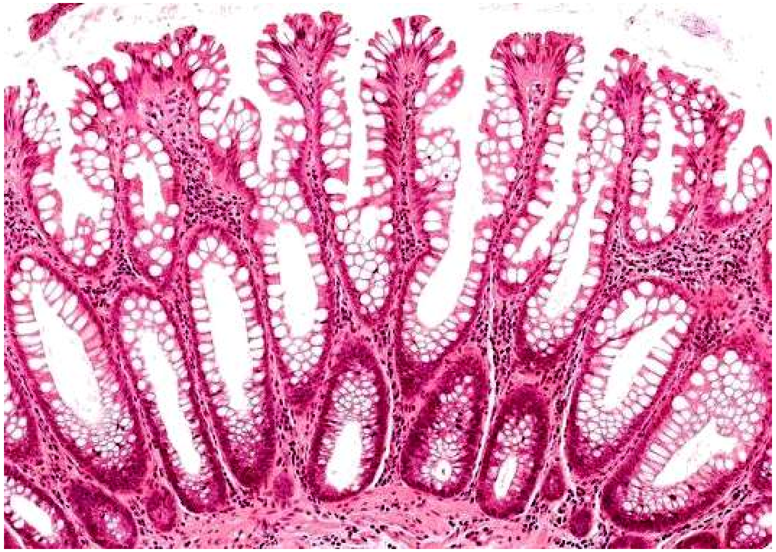
Microvesicular variant is more common and comprises epithelial cells with small mucin vacuoles (related to sessile serrated lesion/polyp)

Goblet cell rich variant is less common and contains prominent goblet cells



Microvesicular hyperplastic polyp (MVHP)

Funnel-shaped crypts with serrations limited to upper two-thirds
Proliferation zone is located uniformly in the basal portion of crypts
Small basally located nuclei, no dysplasia
70–80% BRAF mutated
0% KRAS mutated
+ve CPG island methylation (CIMP +)



Goblet cell-rich hyperplastic polyp (GRHP)

Elongated crypts that resemble enlarged normal crypts with little serrations
Proliferation zone is located uniformly in the basal portion of crypts
Small basally located nuclei, no dysplasia
0% BRAF mutated
50% KRAS mutated
- neg CPG island methylation (CIMP -)

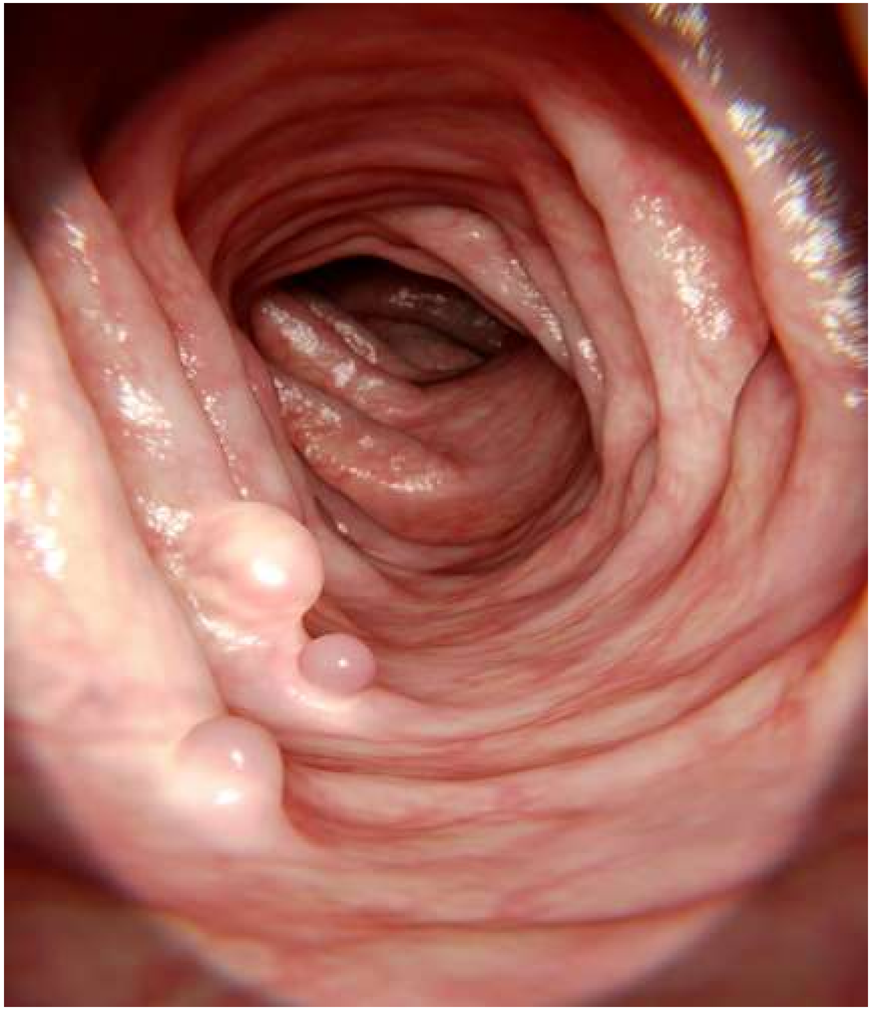
Prognosis of hyperplastic polyp

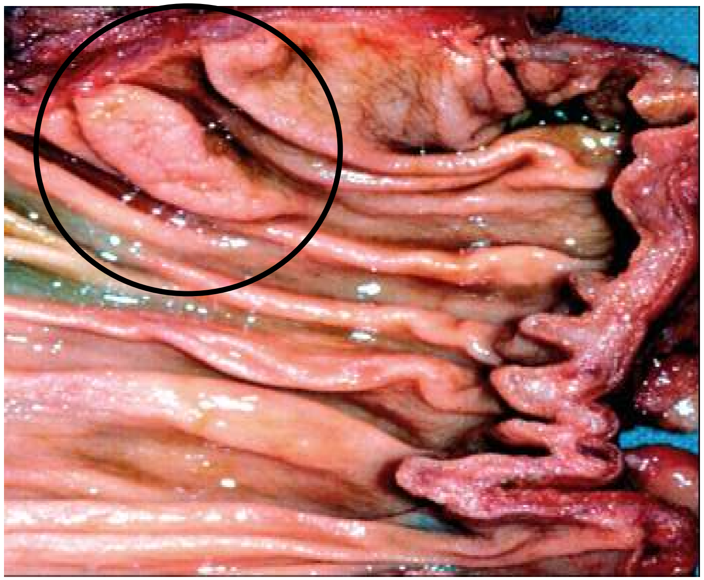
Small distal HPs are considered **benign** and do not affect colonoscopic surveillance intervals

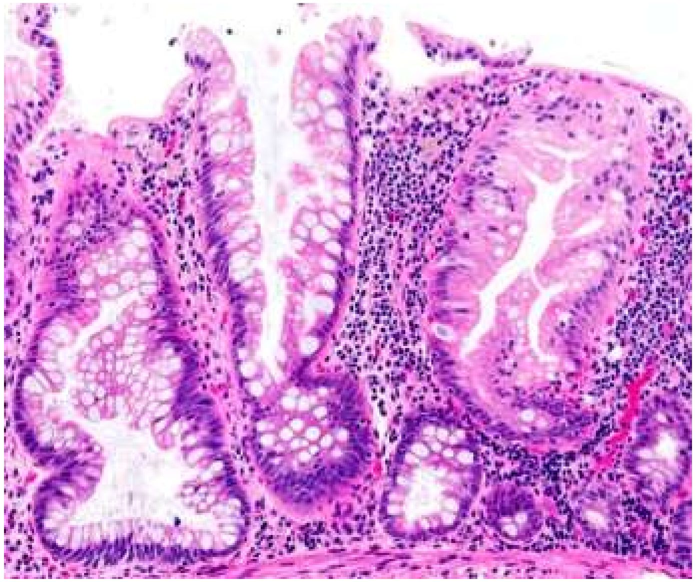
Large (>1 cm) serrated polyps, irrespective of histology increase risk of large metachronous serrated polyp and carcinoma

Recommended **follow-up** intervals are based on low level of evidence and vary by country

Synchronous conventional adenoma may affect surveillance intervals







Sessile serrated lesion
(polyp or adenoma)

Non-dysplastic serrated colorectal polyps

Predilection for the **right colon**

More common among older **women**

Slightly raised pale plaques (slightly yellow owing to a thick layer of mucin)

Often span **>10 mm** and may have a Polyps contain stellate dilated crypts

Precursor to a subset of sporadic **MMR deficient colonic adenocarcinomas**

SSL with dysplasia confers a risk similar to that of comparably sized conventional adenomas

Surveillance guidelines parallel those of conventional adenomas

Sessile serrated lesions

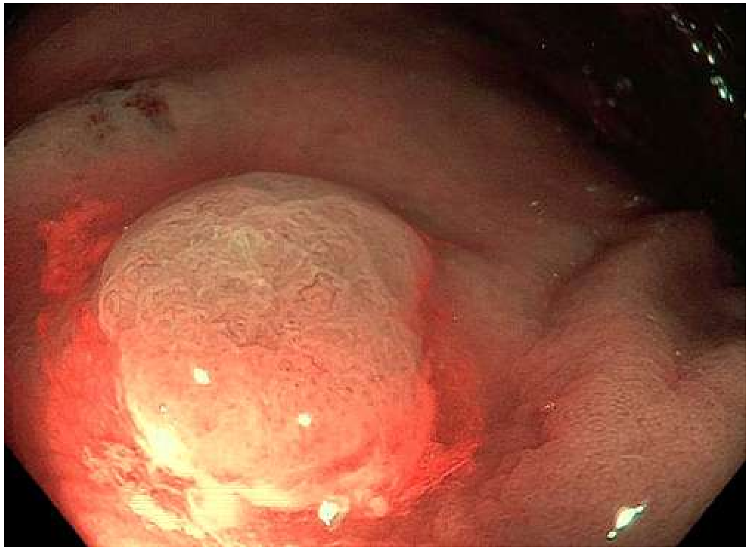
Elongated crypts with prominent infolding of the epithelium and persistent **dilatation in the deep mucosa**

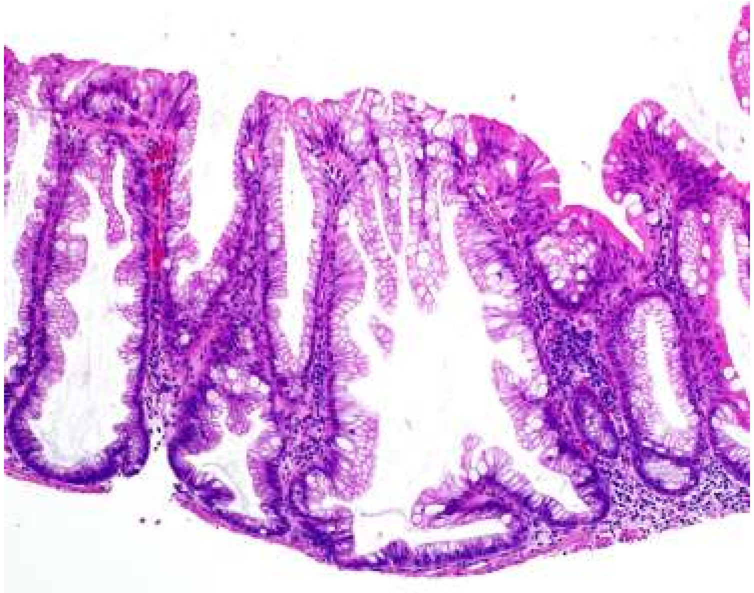
Lesional crypts often show **horizontal growth with branching or budding above the muscularis mucosae**

Greater degree of **Ki-67** nuclear staining than do hyperplastic polyps

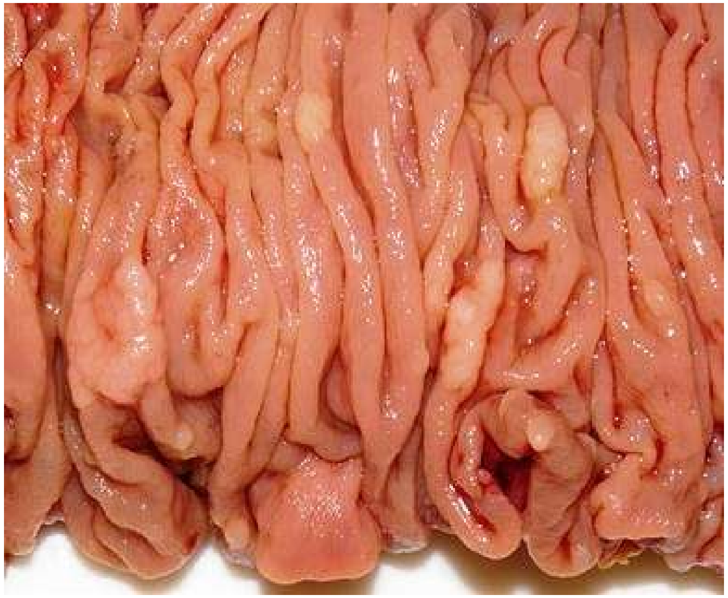
More than 90% of sessile serrated polyps harbor **BRAF mutations**, whereas KRAS mutations are extremely uncommon (<5%)

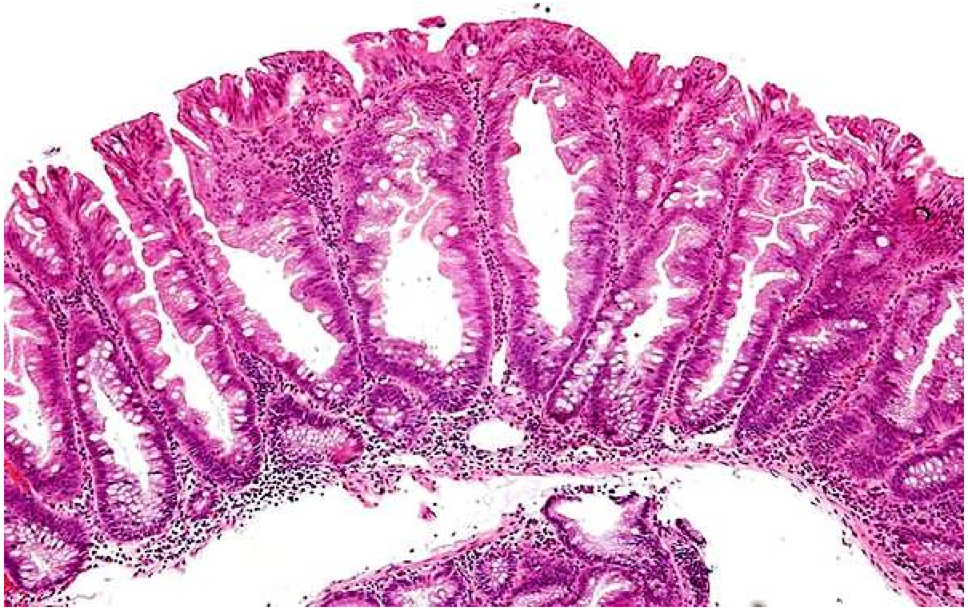
SSP also show frequent CpG island methylation **(CIMP +++)**





Sessile serrated lesion





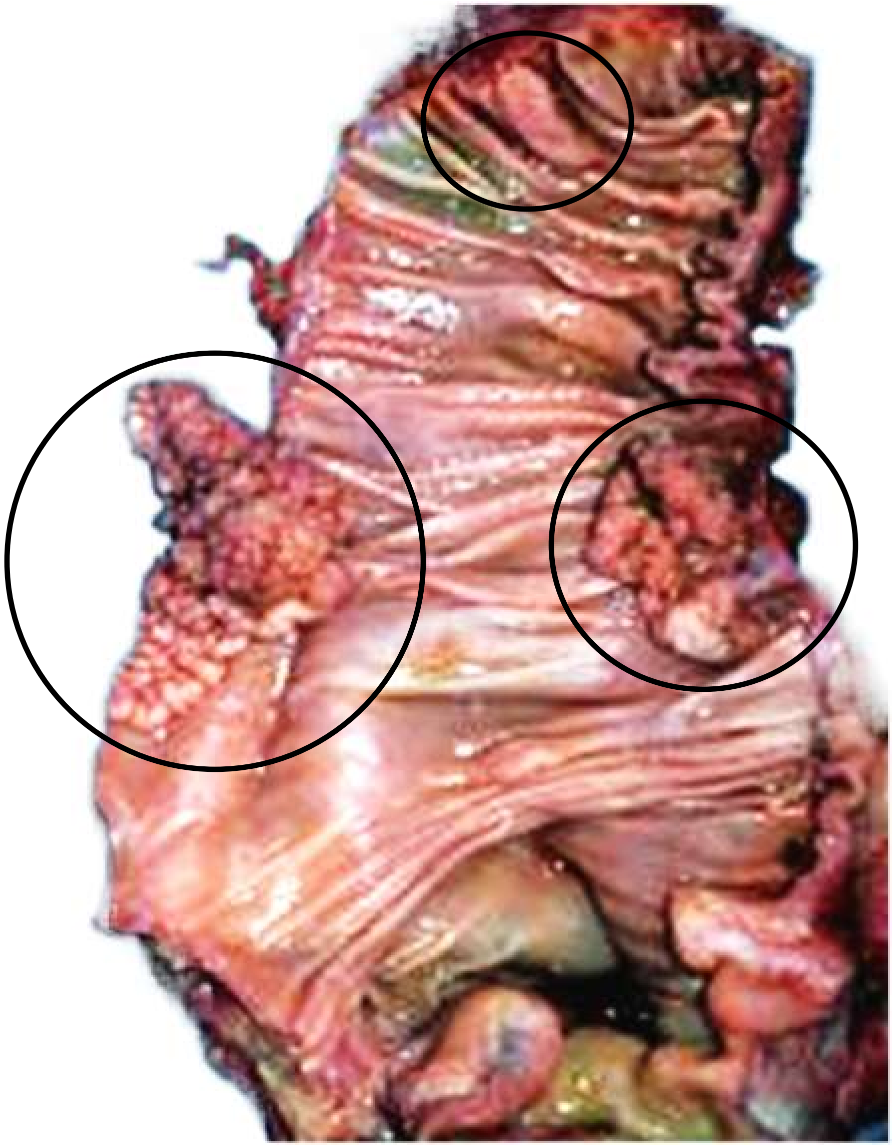
Sessile serrated polyp with dysplasia

<5% of all colorectal serrated polyps and less than 1% of all endoscopically removed lesions

Usually occur in the **right colon** with a predilection for **women >50 years**

Endoscopic appearances are similar to those of sessile serrated polyps

Most dysplastic lesions are **>1 cm**



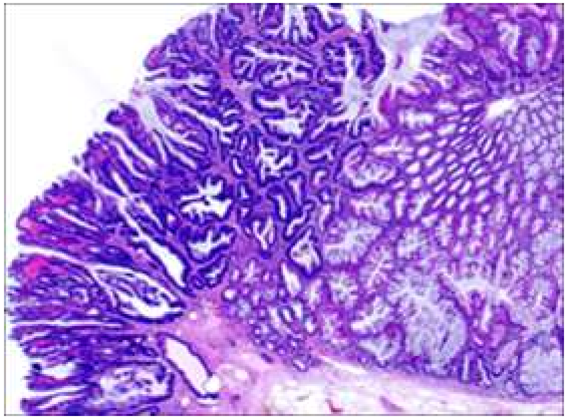
Sessile serrated polyp with dysplasia

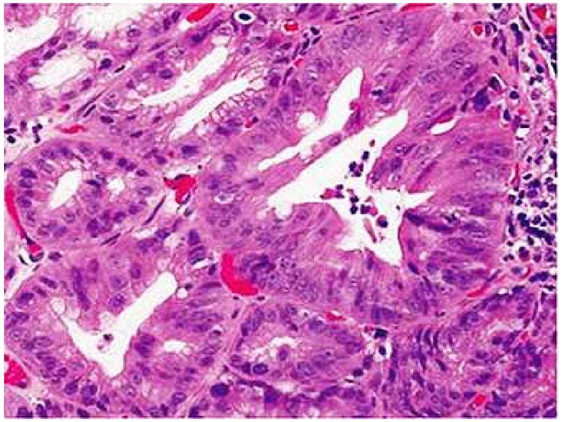
Non-dysplastic sessile serrated polyp with an **abrupt transition to overt dysplasia** (complex architectural abnormalities and low or high grade dysplasia) is characteristic

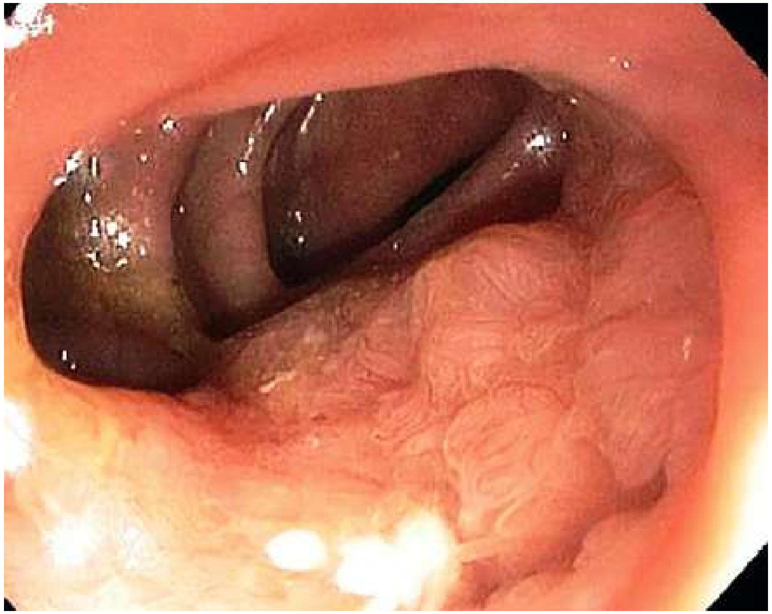
Can have **tubular, tubulovillous or villous architecture** with cuboidal to columnar cells having **eosinophilic cytoplasm and vesicular rounded nuclei**

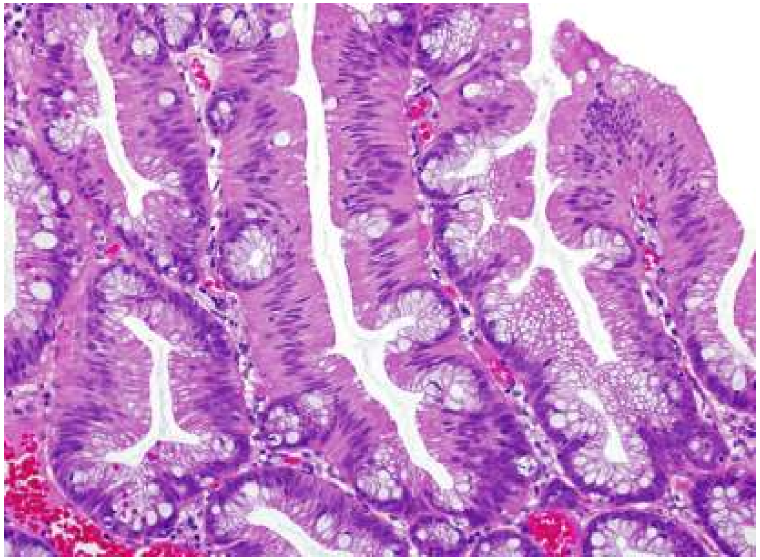
Dysplastic foci usually show either **more or less serration** than adjacent non-dysplastic serrated crypts

>90% BRAF mutated
0% KRAS mutated
+++ CPG island methylation









Traditional serrated adenoma

Uncommon **dysplastic polyps** that account for **<2%** of colorectal adenomas

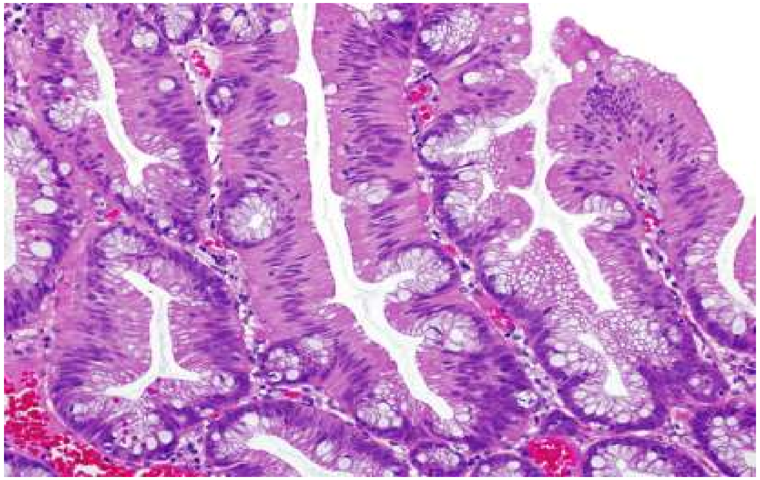
Predilection for the **sigmoid colon and rectum** and is rarely occur in proximal small intestine

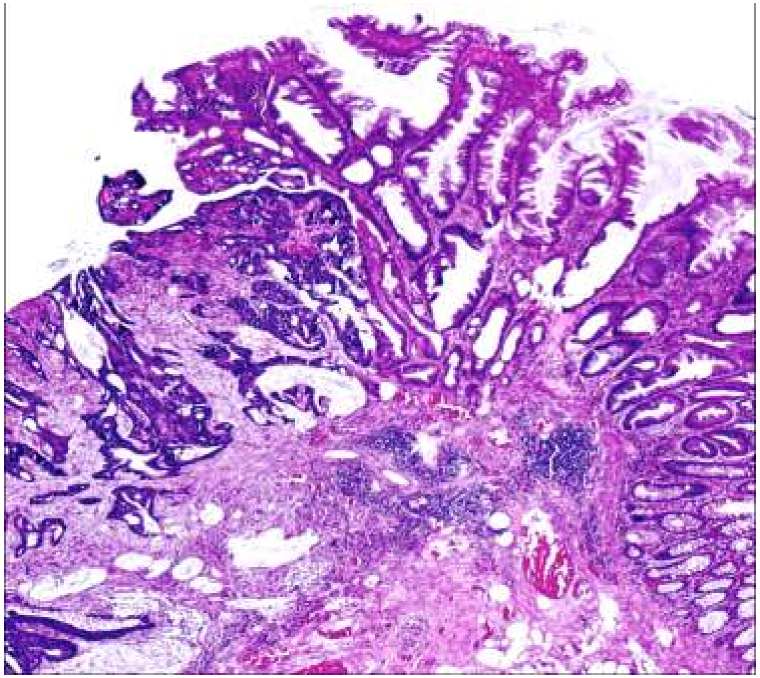
Most are **sporadi**c, but can be familial (described in patients with FAP and serrated polyposis)

Usually **broad-based polyps**

Dysplasia can be **low grade or high grade**

Surveillance guidelines parallel those for conventional adenomas of comparable size



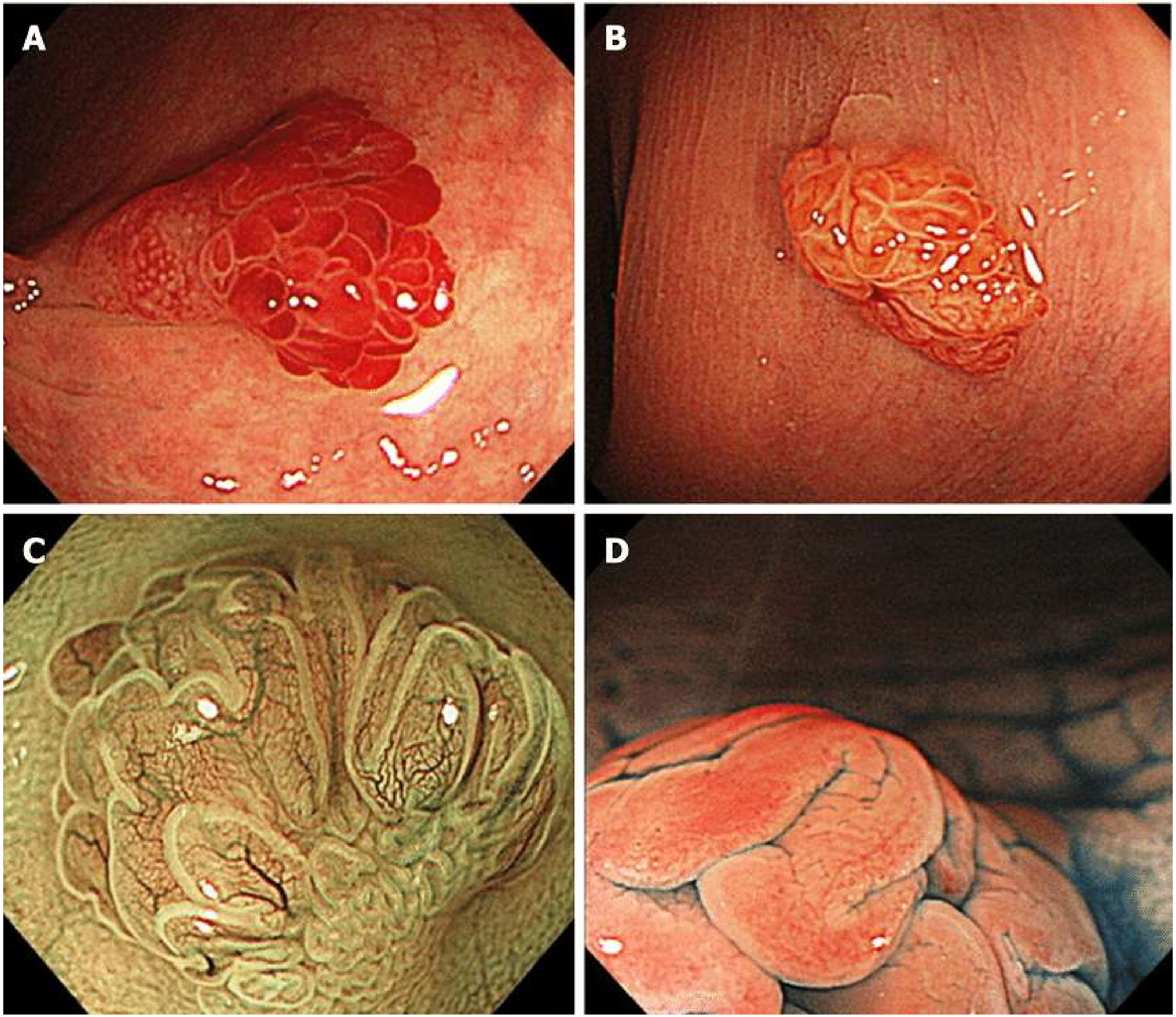


Composed of crypts with slit-like serrations and villi with small invaginations in the epithelium along their **lateral aspects**, which have been termed **aberrant crypt foci**

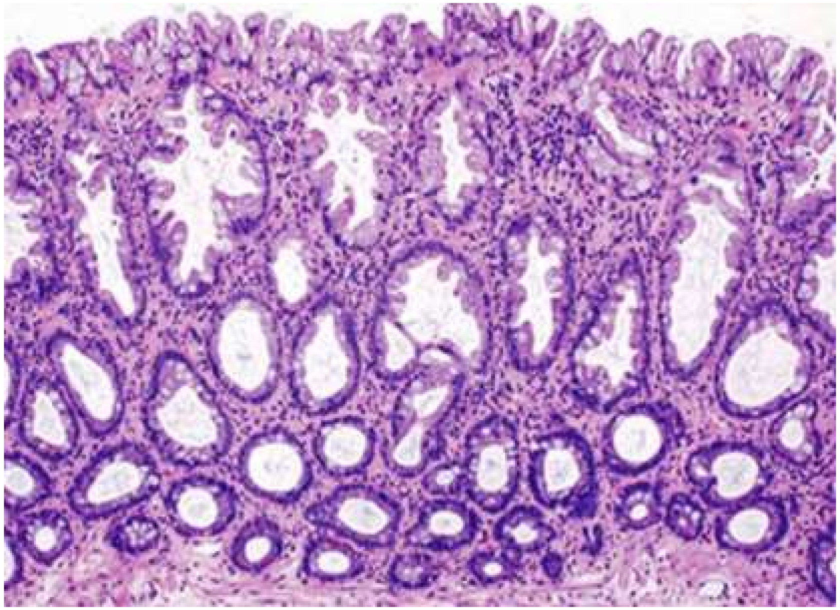
Most show low-grade cytological features with elongated, pencillate nuclei that have smooth contours and small nucleoli

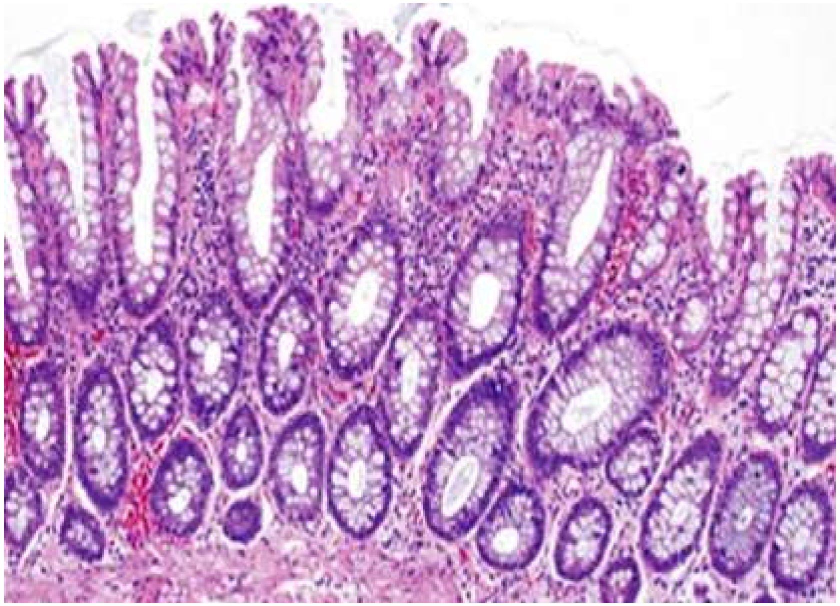
High grade dysplasia and carcinoma are sometimes seen

Traditional serrated adenoma

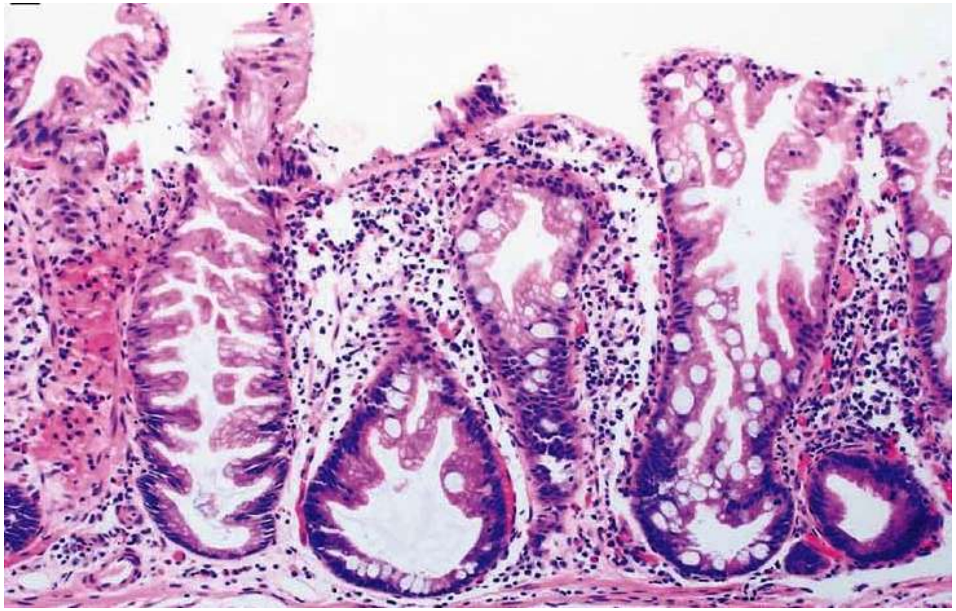


Hyperplastic Polyp

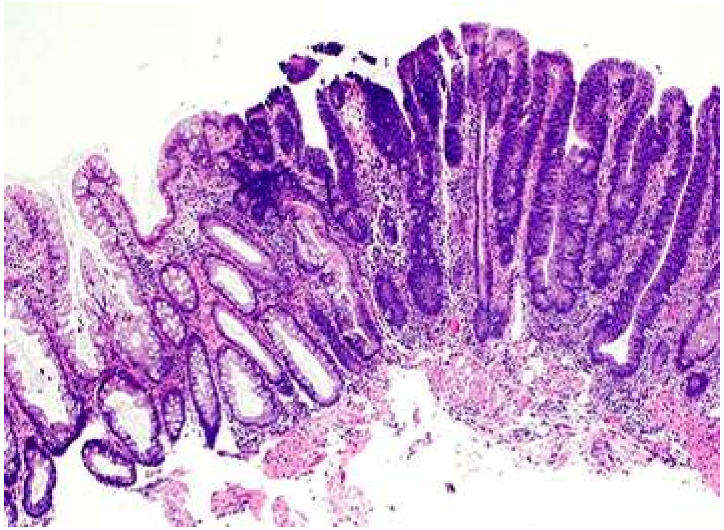


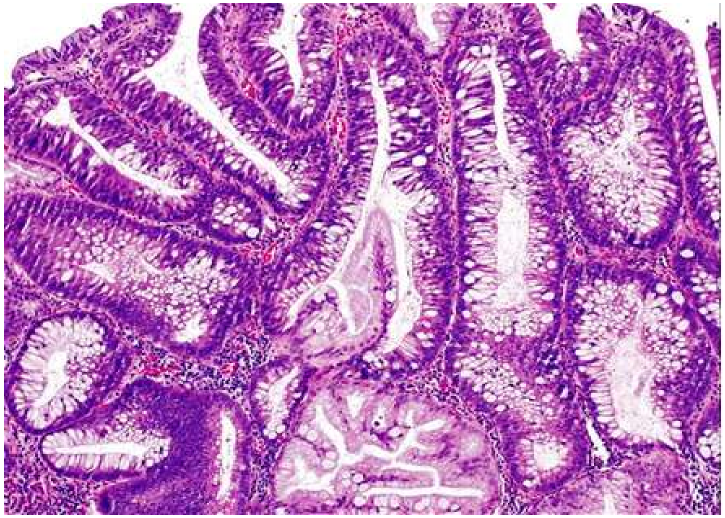


Sessile serrated lesion/polyps

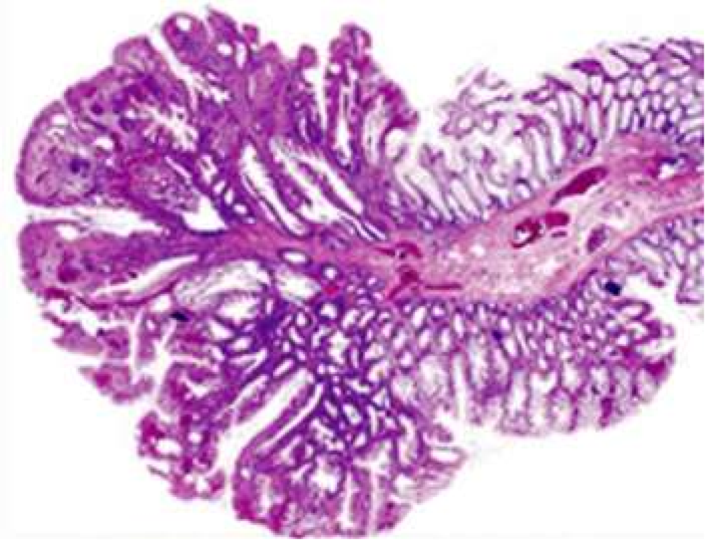


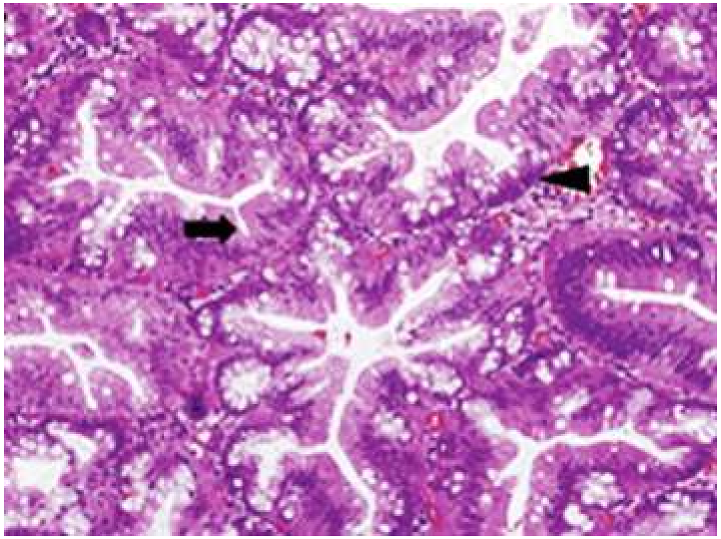
Sessile serrated polyp with dysplasia



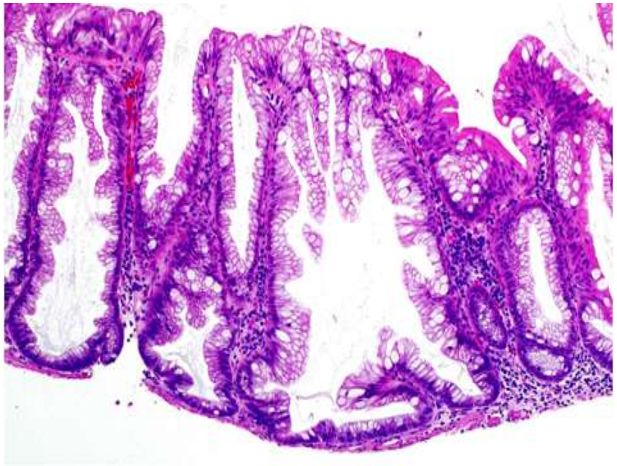


Traditional serrated adenoma

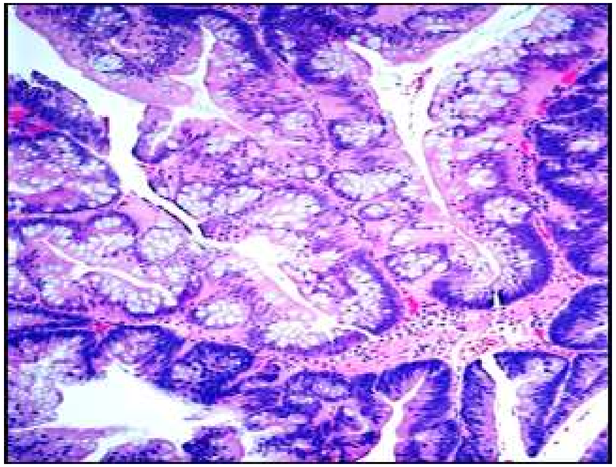




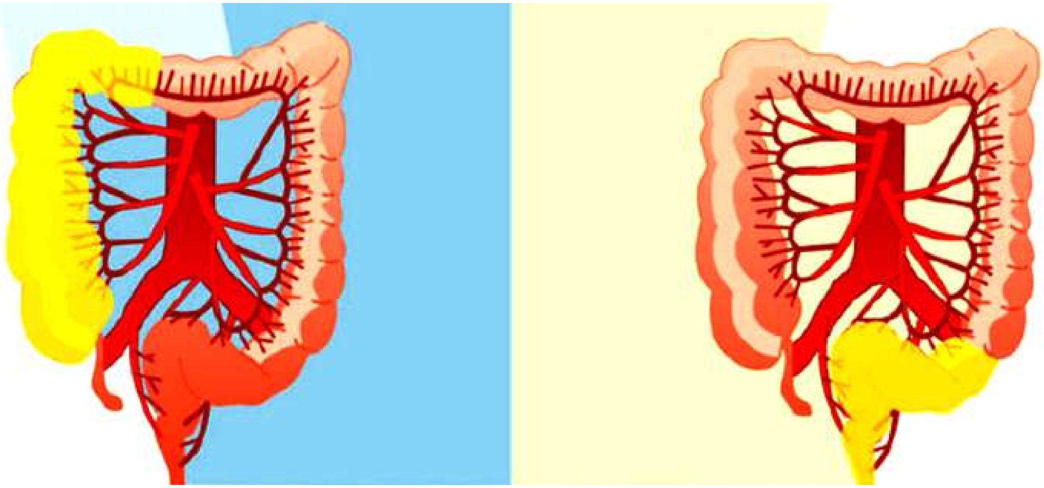
Serrated pathways to colorectal cancers



Sessile serrated polyp
(Proximal colon)



Traditional serrated adenoma
(Distal colon and rectum)



BRAF mutated
MSI-H (CIMP +)

KRAS mutated
MSS (CIMP -)

CpG island methylation (CIMP)

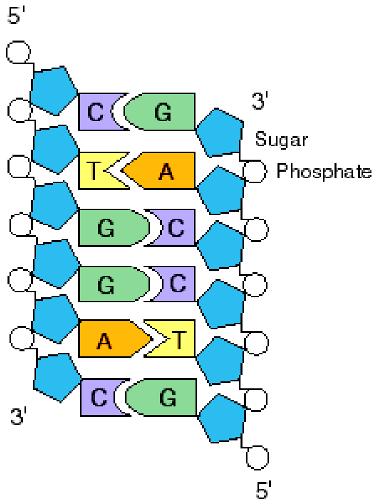
Cytosine and Guanine are linked by phosphate bond (CpG)

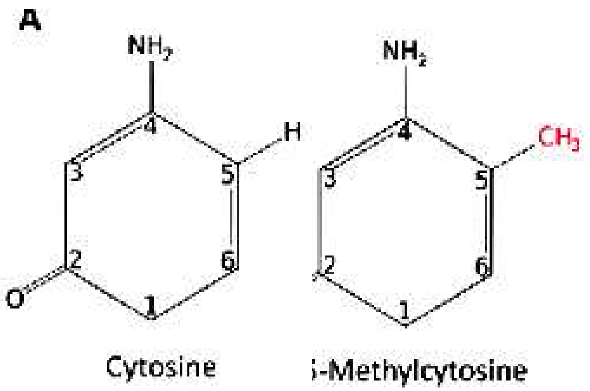
CpG occur **throughout the genome** in groups or regions of **200 bp** or more and are call **CpG islands**

CpG islands are frequently **located in promoter regions associated with tumor suppressor genes**

CpG island methylation (CH_3) can lead to **gene silencing** by physically obstructs the machinery needed to initiate transcription, leading to **tumor suppressor genes inactivation**

Adenine (A)
Thymine (T)
Cytosine (C)
Guanine (G)





Serrated lesions of the colorectum
35% of colorectal polyps

Hyperplastic polyps 25%	Sessile serrated lesions 10%	Traditional serrated adenoma 1%
Distal colon and rectum	Proximal colon	Distal colon and rectum
<5mm	5mm->10mm	>10mm
Sessile	Sessile	Sessile or pedunculated
Pale, round or oval	Irregular shape with mucus cap	Multilobated pine-cone appearance
Narrow, uniform basal crypts with superficial serration	Serration extending to base of crypts with branching and boot-shaped basal crypts	Pseudostratification with villous pattern, cytoplasmic eosinophilia and ectopic crypts

Serrated polyposis

Definition

Multiple large (>5mm) hyperplastic polyps proximal to the sigmoid colon, 2 of which at least 10mm

At least 20 serrated polyps of any size distributed throughout the colorectum, including five proximal to the rectum

Exact genetic basis is unknown with no underlying germline abnormalities (multiple genes and environmental factors may be involved)

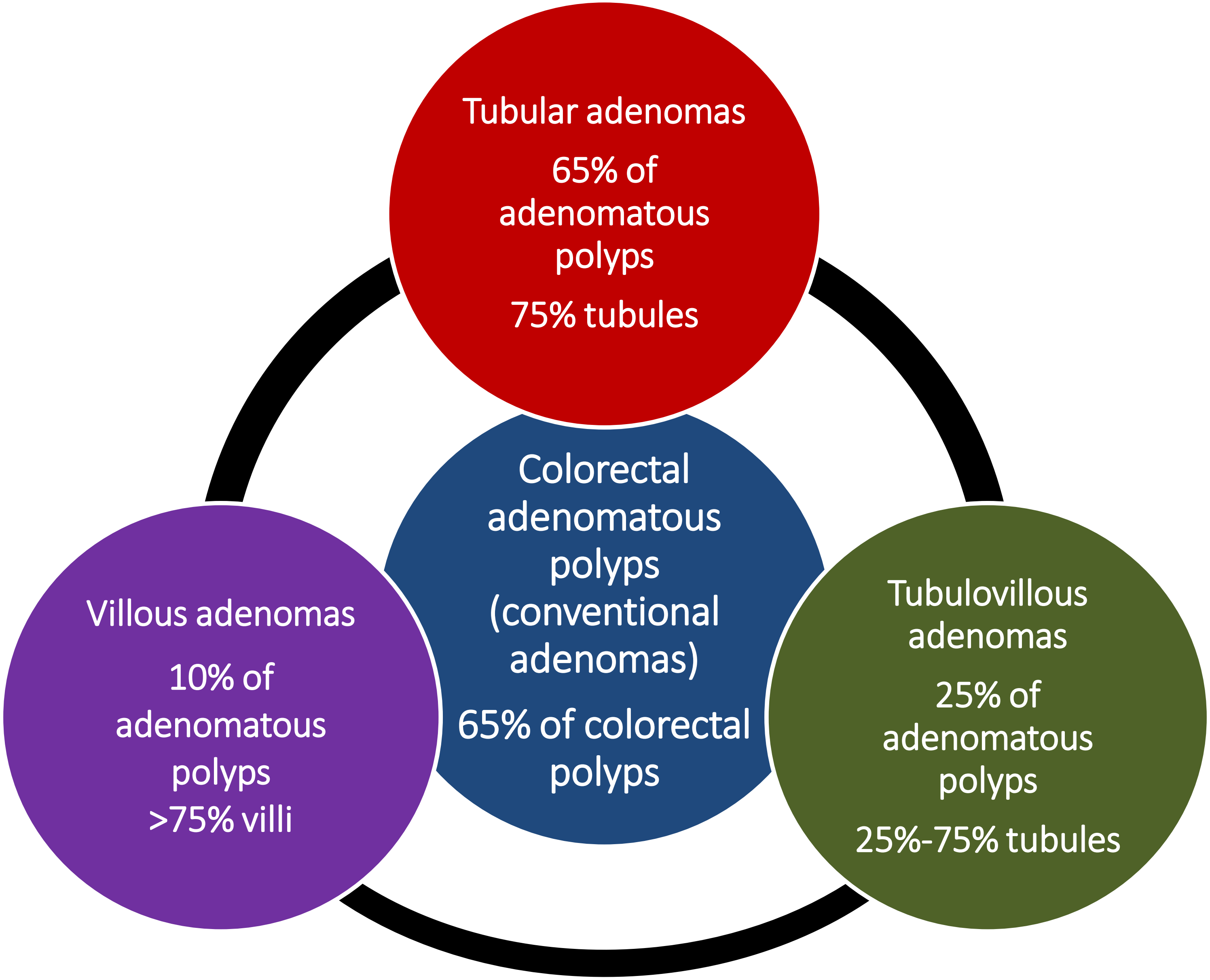
Older adults with equal gender distribution

Disease criteria rest on the **cumulative number of polyps**, rather than polyp detection during a single colonoscopy

Environmental factors associated with serrated polyposis include **cigarette smoking and obesity**

Overall cancer risk is estimated to be 10% at 5 years

Patients can often be managed with **serial colonoscopies and polyp removal**


Tubular adenomas
65% of adenomatous polyps
75% tubules
Colorectal adenomatous polyps (conventional adenomas)
65% of colorectal polyps
Villous adenomas
10% of adenomatous polyps
>75% villi
Tubulovillous adenomas
25% of adenomatous polyps
25%-75% tubules

Conventional adenoma

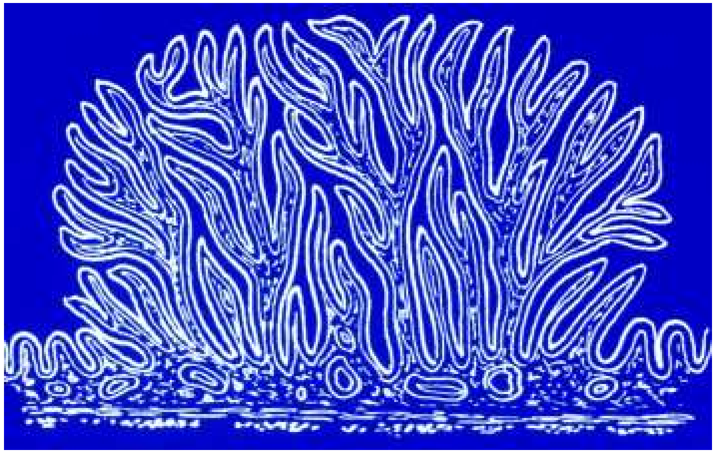
Clonal neoplasms composed of **dysplastic epithelium**

Classified based on **gross and histological features**

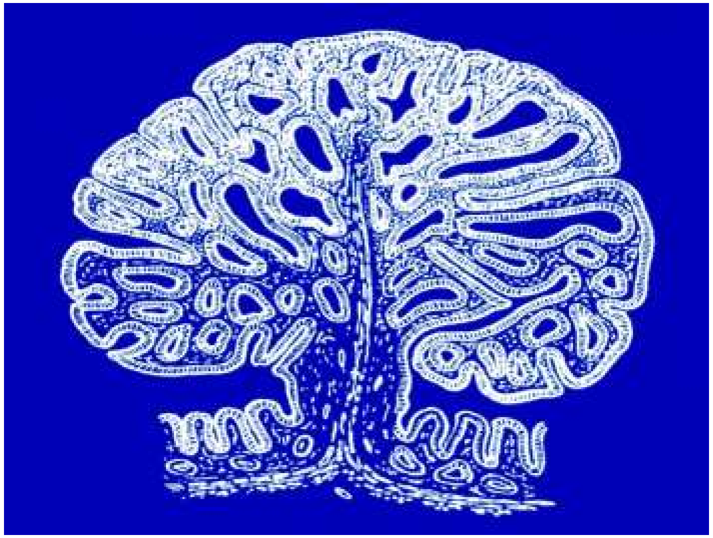
Macroscopically polyps can be **pedunculated or sessile** based on the presence or absence of a **stalk**

Microscopically polyps can be **tubular, villous or tubulovillous** based on the relative amounts of these components within the polyp

Clinically important because they are **precursors to carcinoma**



Broad based (sessile) villous adenoma



Pedunculated tubular adenoma

Conventional colorectal adenomas

More common in **western countries** than developing parts of the world

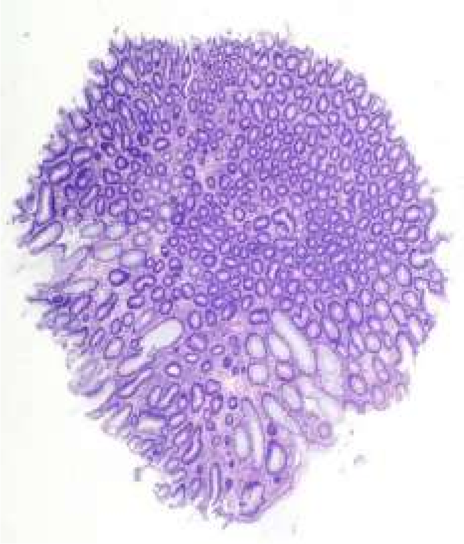
Conventional adenomas account for **65% of all endoscopically removed colorectal polyps**

Small adenomas are evenly distributed throughout the colorectum, whereas **larger adenomas are more commonly located in the distal colon**

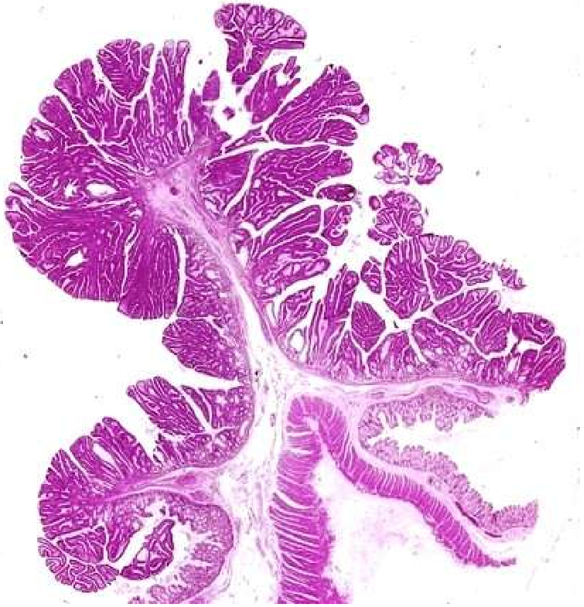
Cancer risk in polyps is related to the **size and number of polyps and high grade dysplasia**

Invasive carcinoma is detected in 0.5% of adenomas smaller than 10 mm, 5% of adenomas that range from 10 to 20 mm, and 10% of adenomas larger than 20 mm

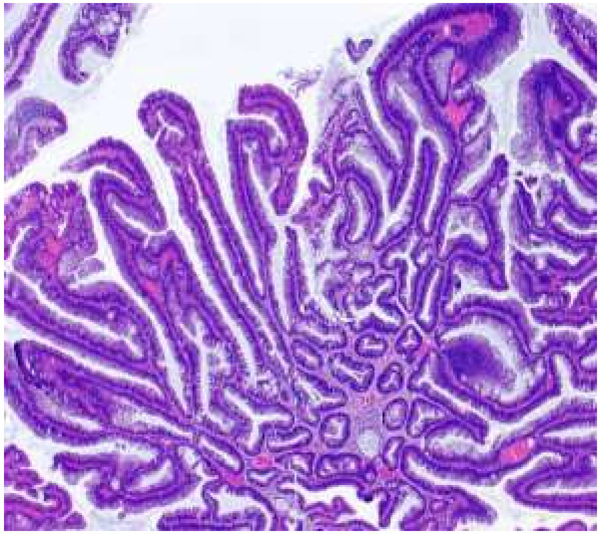
Tubular adenoma

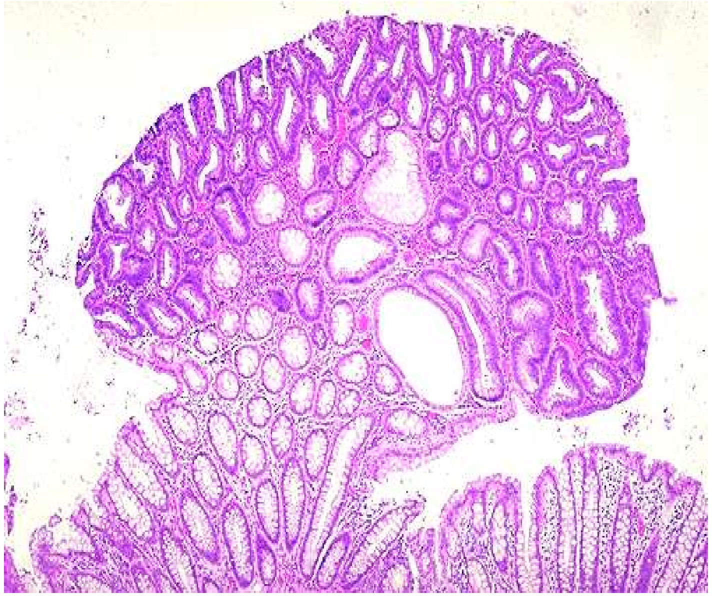


Tubulovillous adenoma



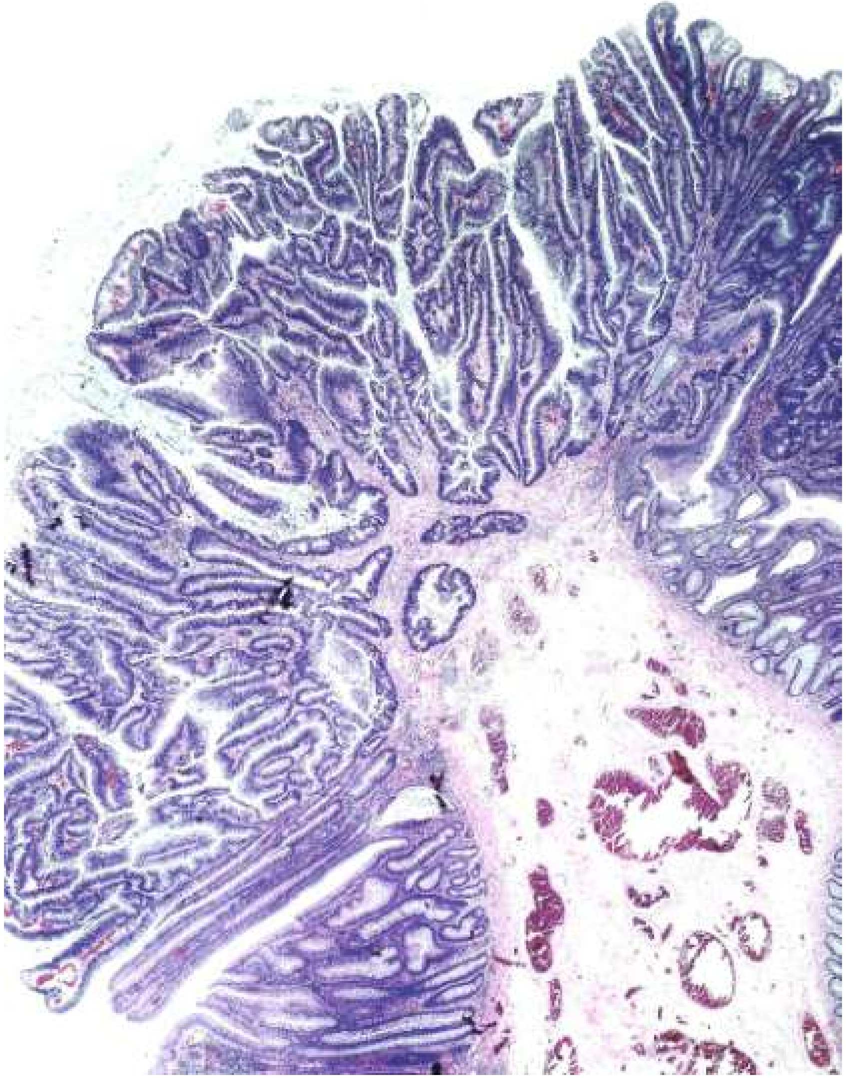
Villous adenoma

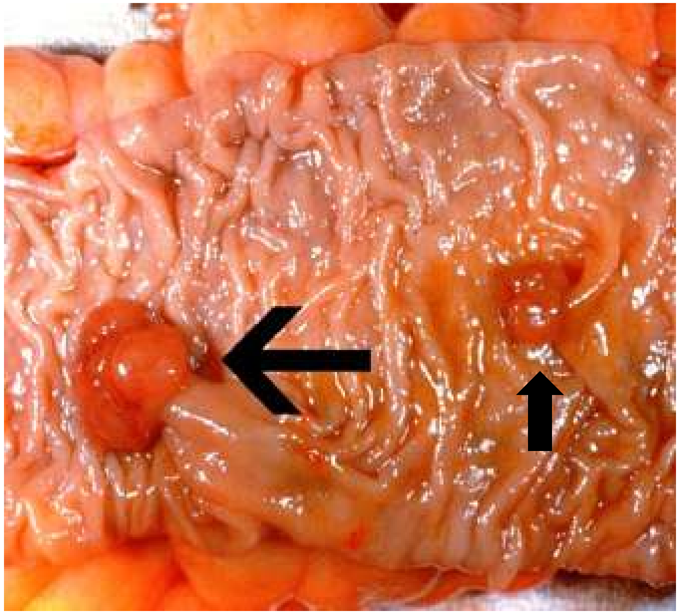




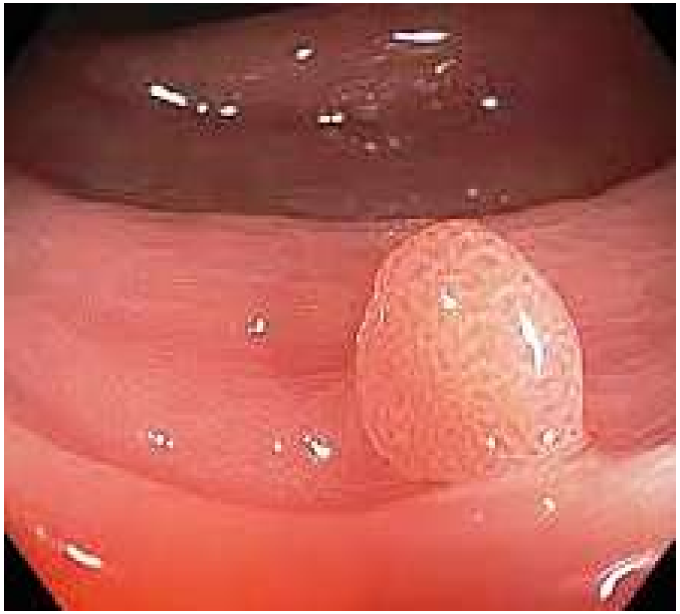
Low grade dysplasia in a pedunculated tubular adenoma

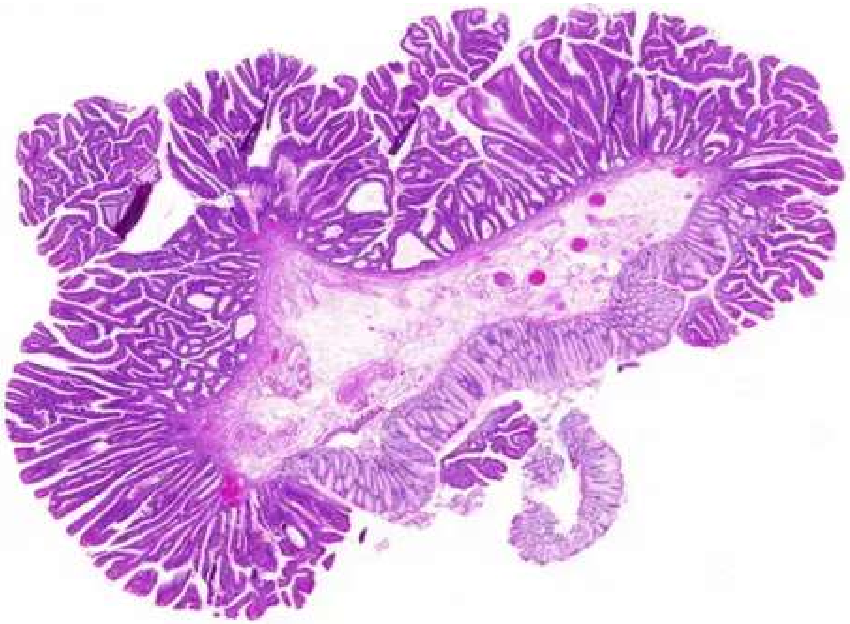
High grade dysplasia in a sessile tubulovillous adenoma





Conventional colorectal adenomas

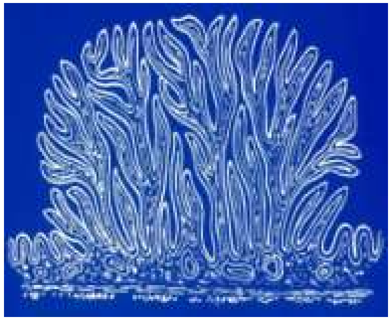




Villous adenoma

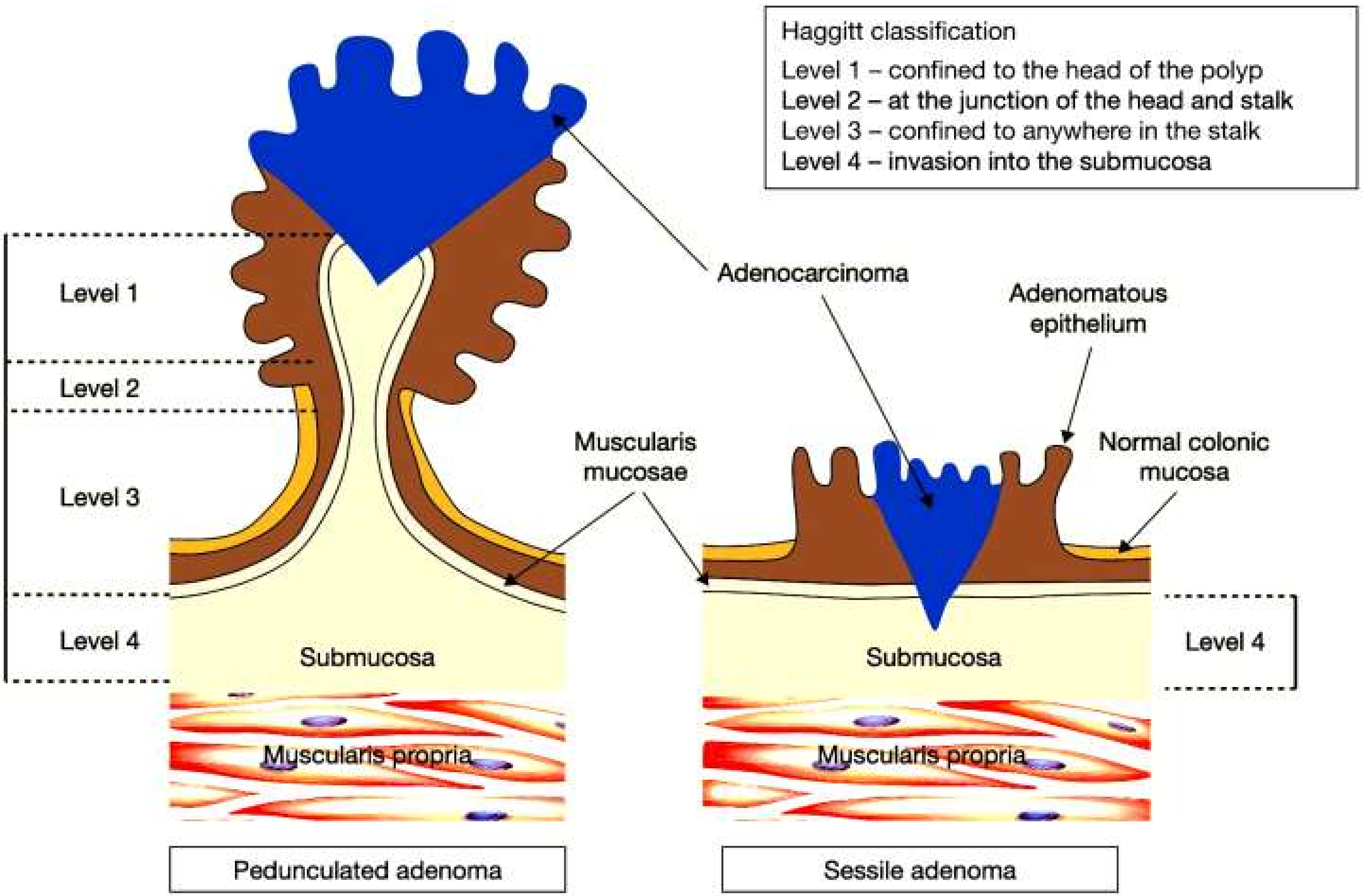
Adenoma-carcinoma sequence (progression to cancer)

- Size: >20 mm
- Type: Villous/tubulovillous
- Dysplasia: High grade
- Number: Multiple
- Shape: Sessile



Cancer in adenomatous polyp

The Haggitt classification of depth of invasion in malignant pedunculated and sessile polyps



Note, a sessile polyp has no stalk therefore automatically classified as a Haggitt 4)[18]

Dr. Roger Haggitt was shot and killed on June 29, 2000, by a pathology resident dismissed for poor performance.

Familial adenomatous polyposis

Autosomal dominant polyposis syndrome

Mutations in the **APC gene**

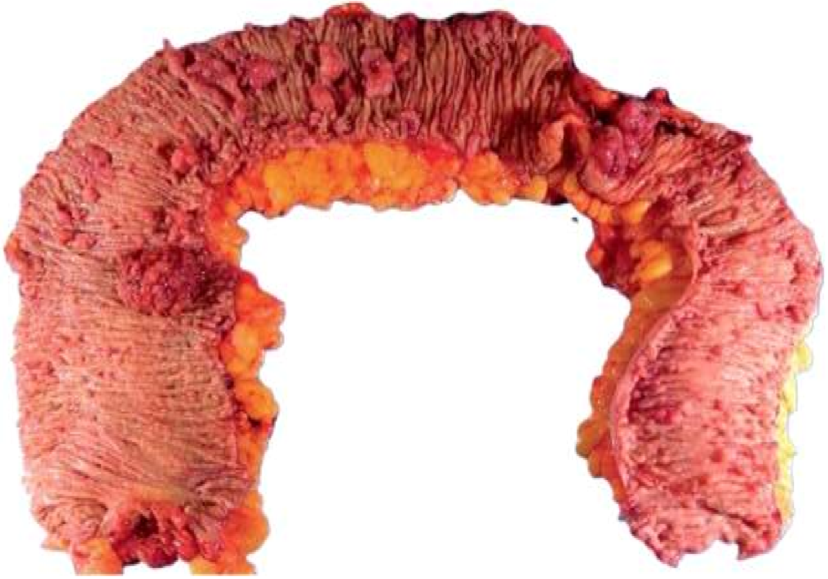
Hundreds to thousands of polyps **throughout the GI**

High lifetime risk of CRC if left untreated

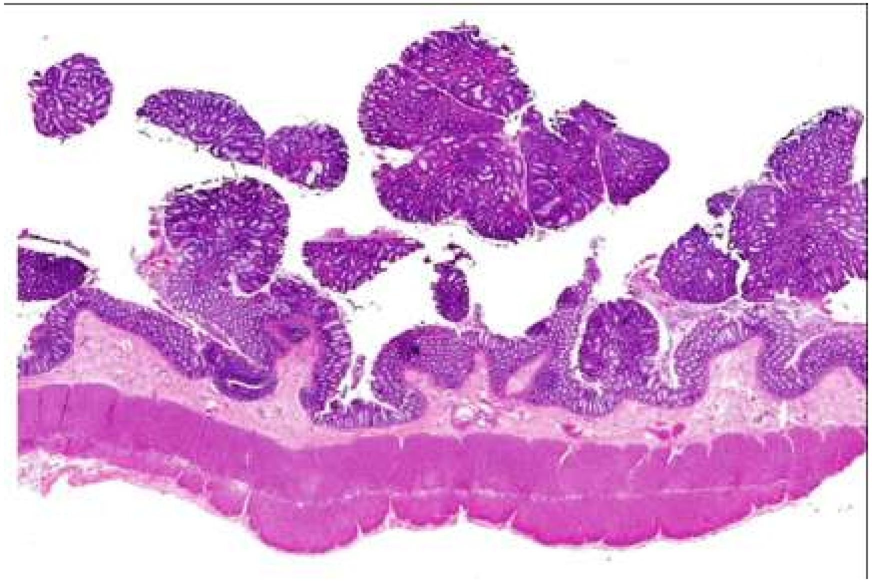
Commonly develop **gastric and duodenal polyps and cancers , desmoid fibromatosis, hepatoblastoma and thyroid cancer**

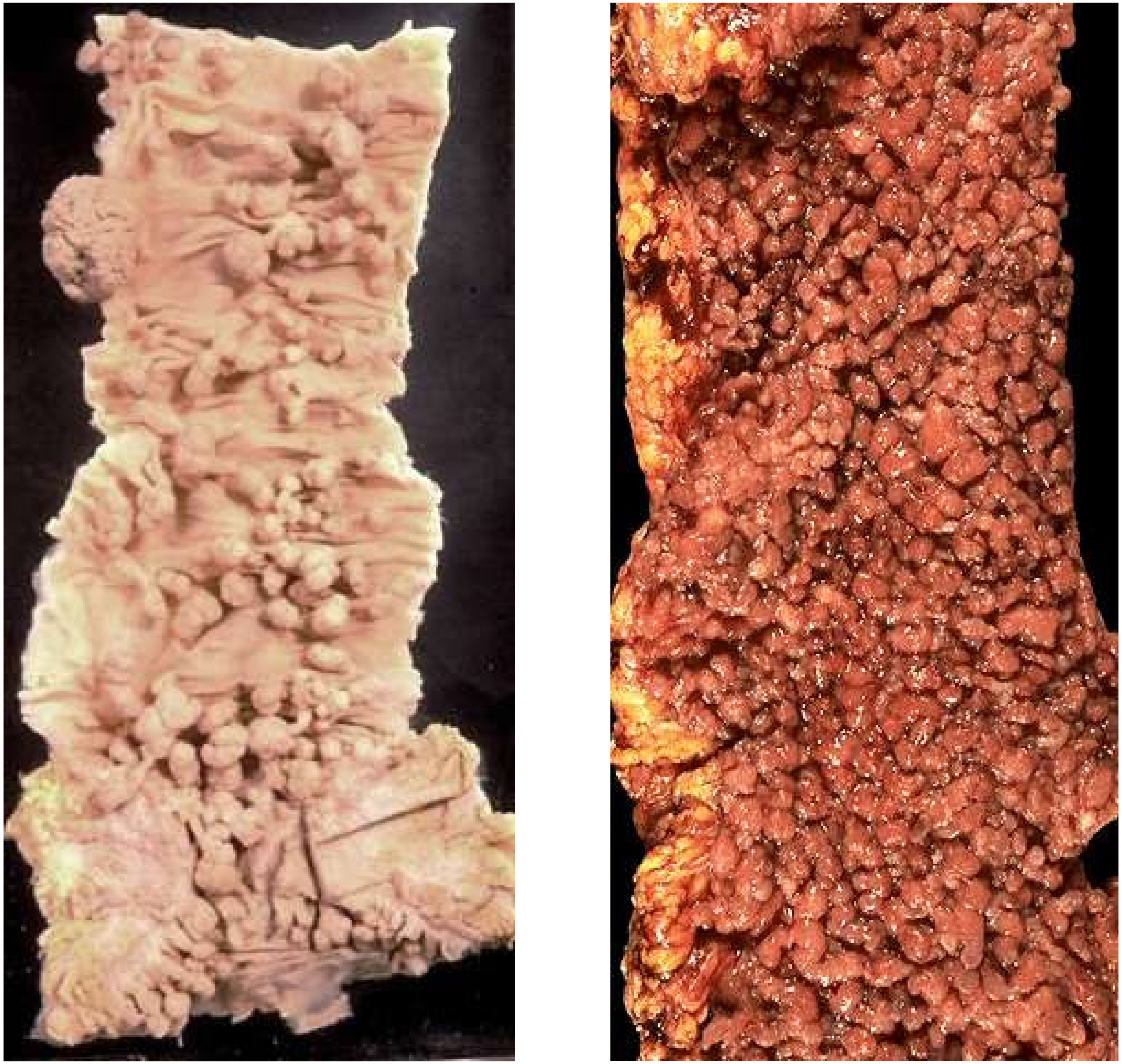
Colectomy is a primary intervention offering substantial risk reduction for CRC development

Screening for associated cancers to enable early detection and intervention

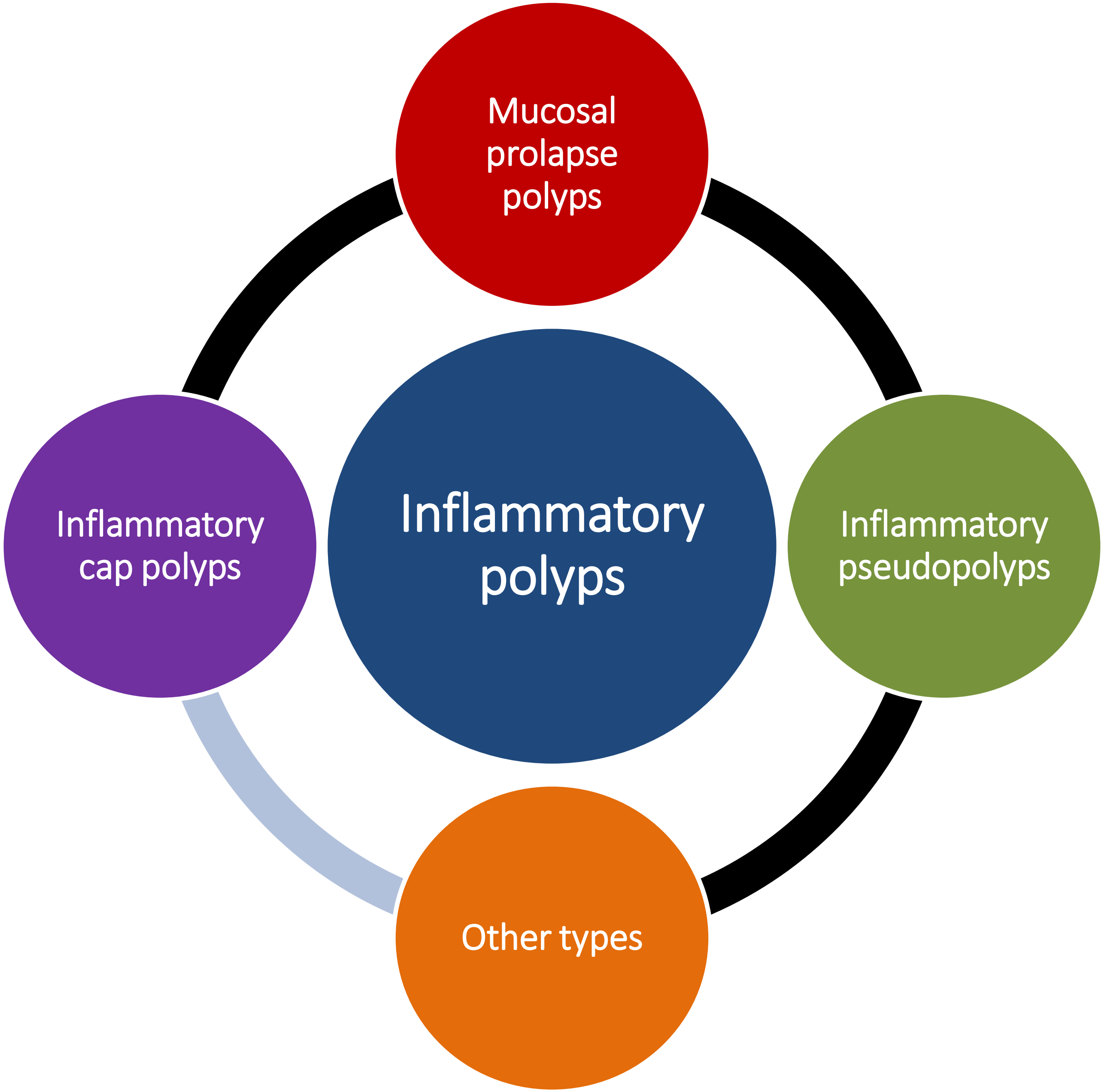


Familial adenomatous polyposis





Familial adenomatous polyposis


Mucosal prolapse polyps
Inflammatory cap polyps
Inflammatory polyps
Inflammatory pseudopolyps
Other types

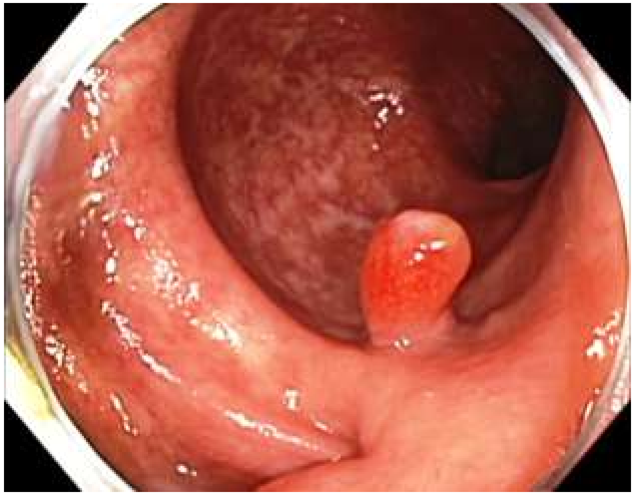
Inflammatory polyps general consideration

Non-neoplastic intraluminal projections often with surface ulceration

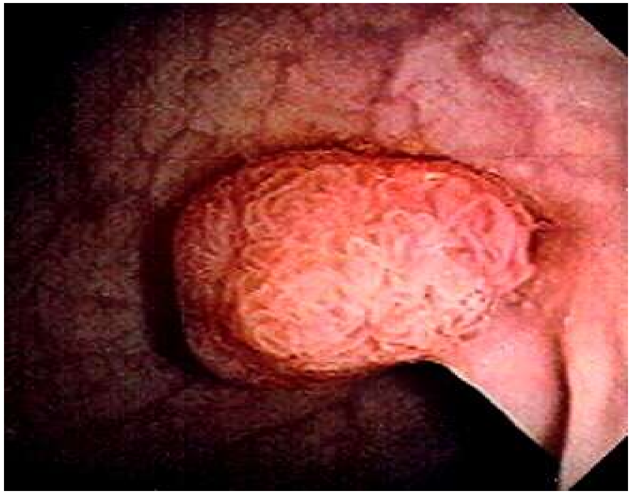
Inflammatory polyps are composed of **granulation tissue together with stroma, epithelium and inflammatory cells**

Inflammatory polyps include

- **Inflammatory pseudopolyps**
- **Inflammatory cap polyps**
- **Prolapse type polyps**
- **Other types**



Inflammatory pseudopolyps



Prolapse polyp

Subtypes of inflammatory polyps

Inflammatory pseudopolyps

IBD associated polypoid inflammatory granulation tissue

Inflammatory cap polyp

Polyp that forms at the **edge of ulcers**

Prolapse associated polyp

Polyp that develops in areas of **mucosal prolapse**

Solitary rectal ulcer syndrome (SRUS)

Inflammatory cloacogenic polyps (ICP)

Inflammatory myoglandular polyp (IMGP)

Proctitis cystica profunda (PCP)

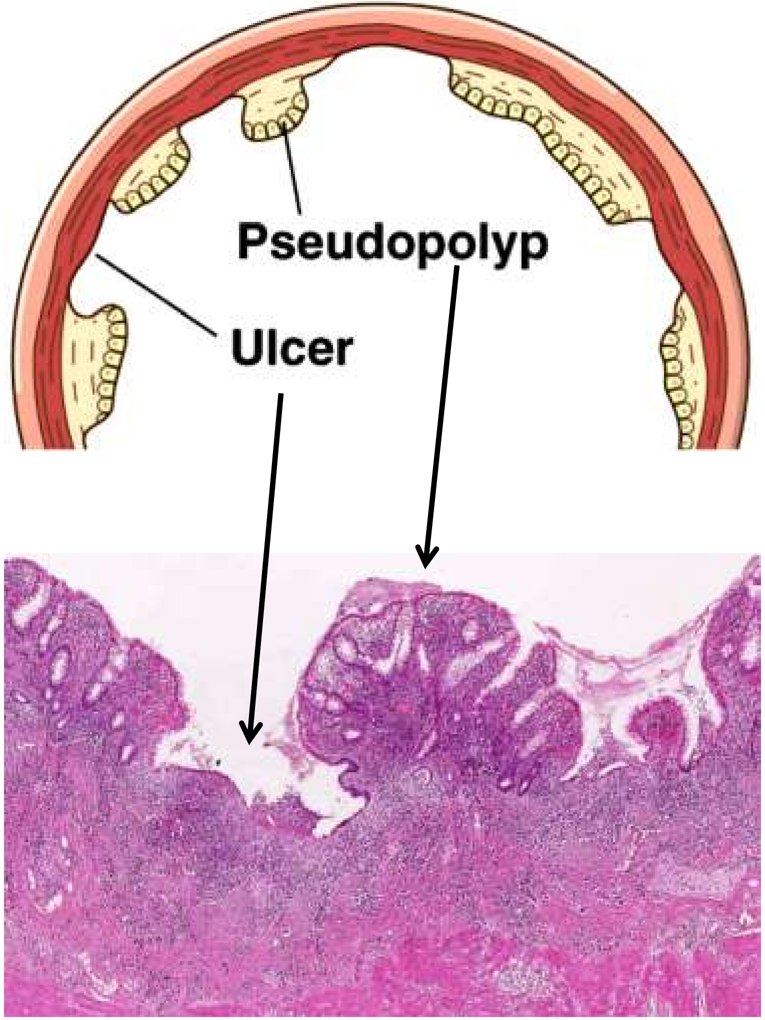
Inflammatory pseudopolyps

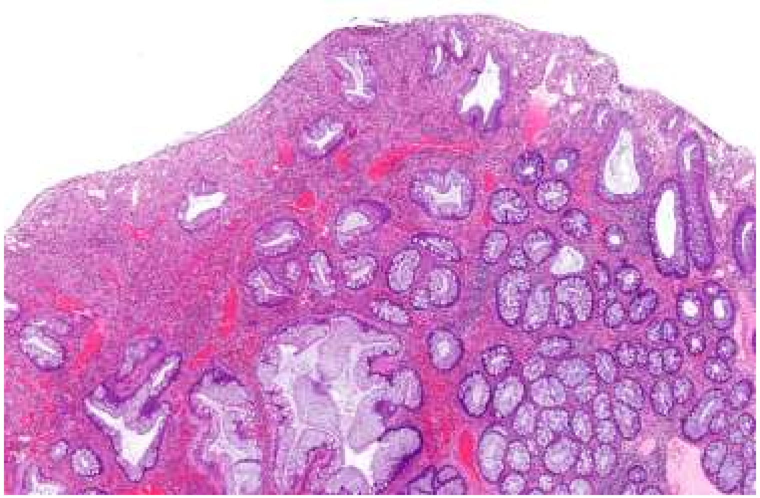
Non-neoplastic lesions originating from the mucosa after repeated periods of **inflammation and ulceration** associated with excessive healing processes

Occur in **ulcerative colitis** more often than in Crohn disease

Found more often in **colon** but have been detected in **other parts of the GI tract**

Larger polyps exceeding 1.5 cm, they are classified as **giant pseudopolyps**



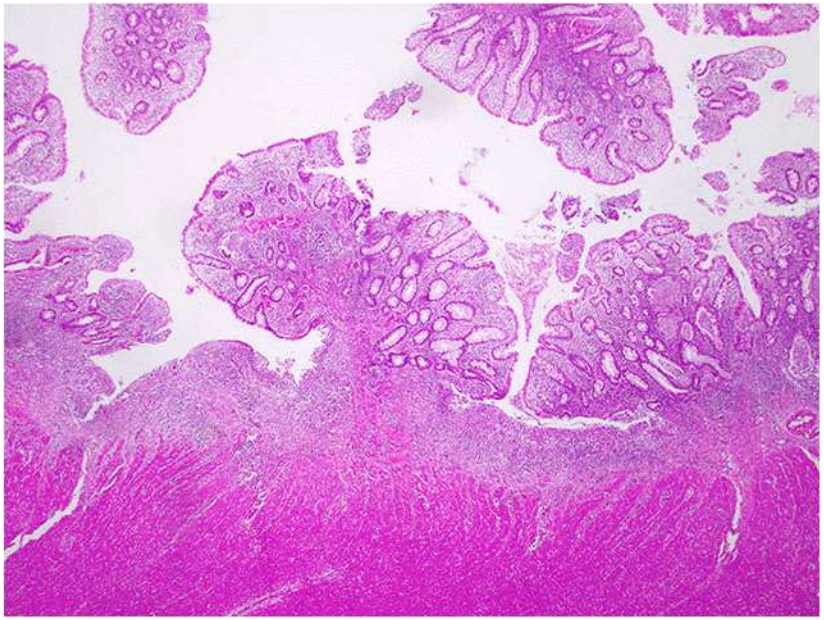


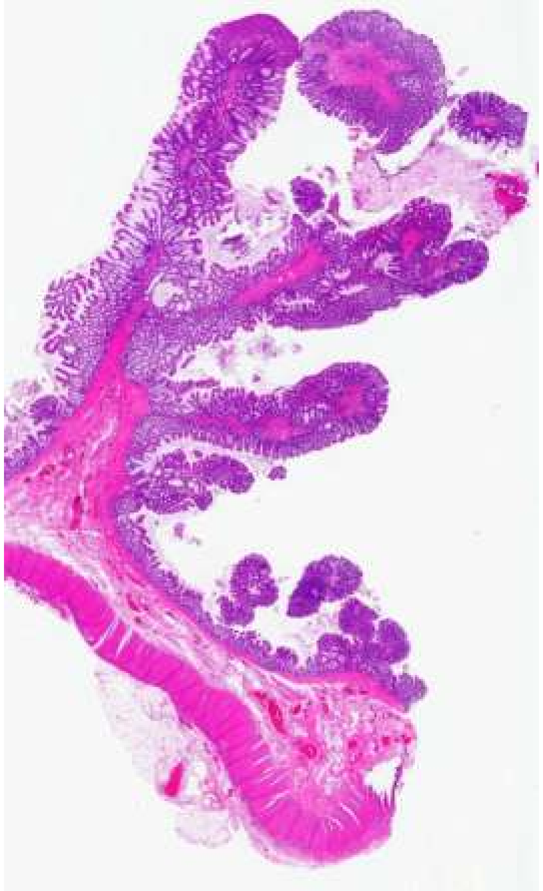
Inflammatory pseudopolyps

Islands of residual intact colonic mucosa that are the result of **ulceration and regeneration** that occurs in response to localized or diffuse inflammation (ulcerative colitis or Crohn disease)

The distinctive histological features **include mixed inflammatory infiltrates, erosion and epithelial and stromal hyperplasia**

Inflammatory pseudopolyps





Filiform polyps/polyposis (FP)

Multiple slender worm-like projections consisting of submucosal fibrovascular accentuation within normal or inflamed mucosa

Vast majority of cases occur in the setting of inflammatory bowel disease, particularly UC

Pathogenesis is uncertain but long-term inflammation with alternating periods of ulceration and healing may lead to the formation of finger-like projections

Mostly asymptomatic but anemia, weight loss, pain and diarrhea, obstruction and intussusceptions may be seen

Inflammatory cap polyposis

Inflammatory polyps with a “cap” of fibrinopurulent granulation tissue

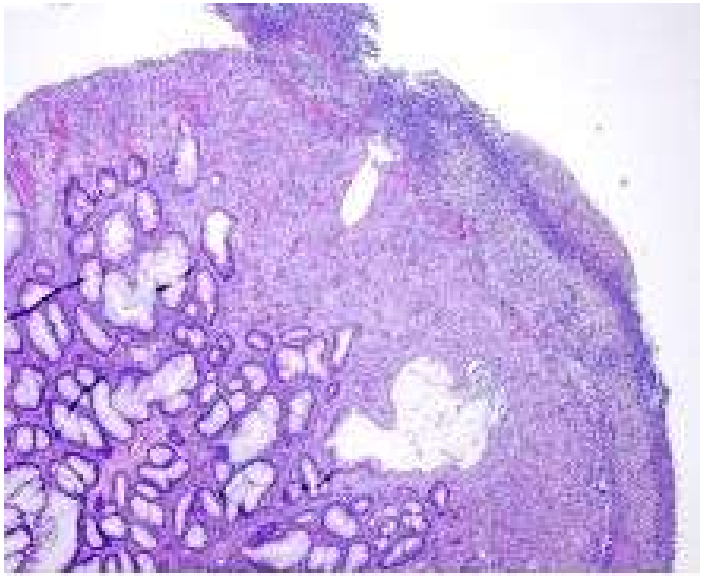
Solitary or multiple ulcerated polyps usually in the left colon

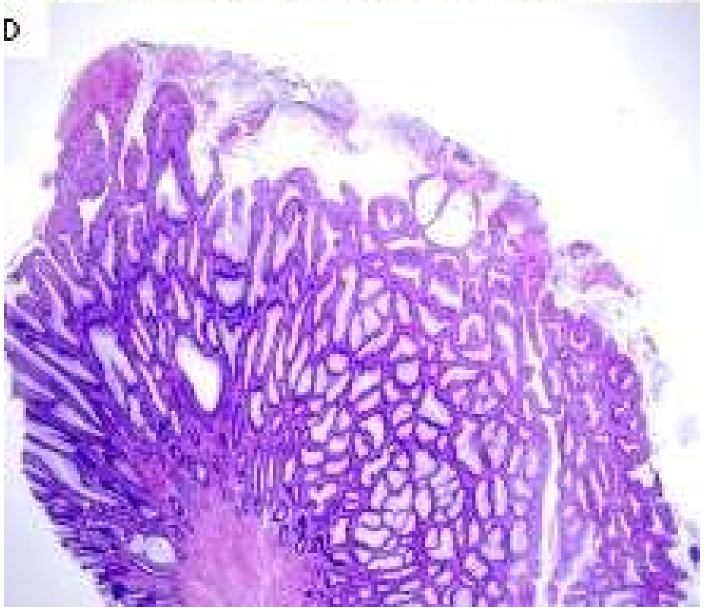
Dilated **superficial crypts** containing mucus and inflammatory cells embedded in florid granulation tissue

Deep crypts show **hypermucinous epithelium**

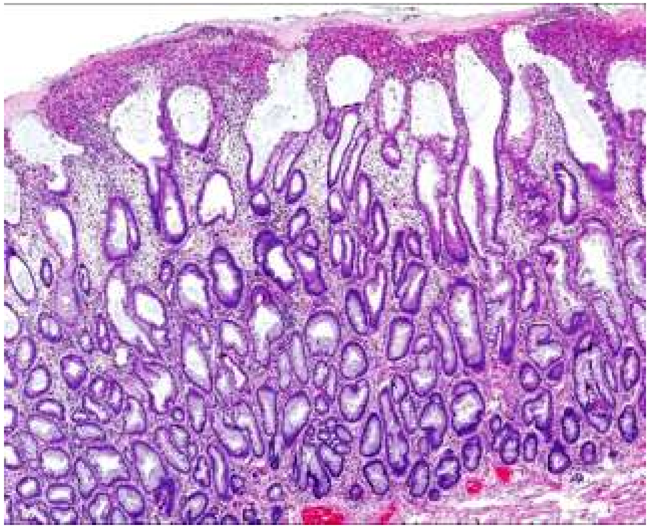
Present with **mucoid diarrhea, rectal bleeding and tenesmus anemia**

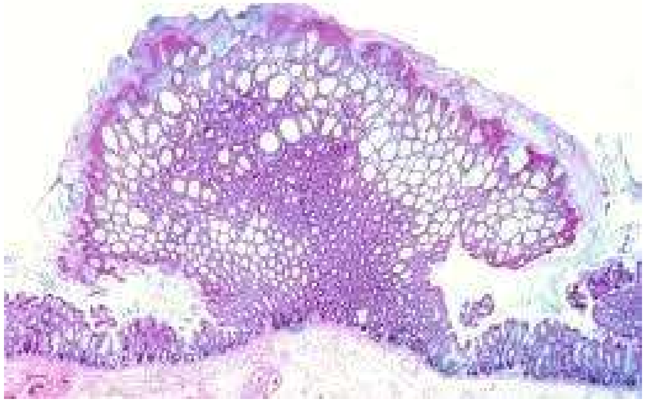
Etiology is unknown but **abnormal colonic motility and repeated trauma** to the colonic mucosa by straining at defecation seems to be the cause in most patients

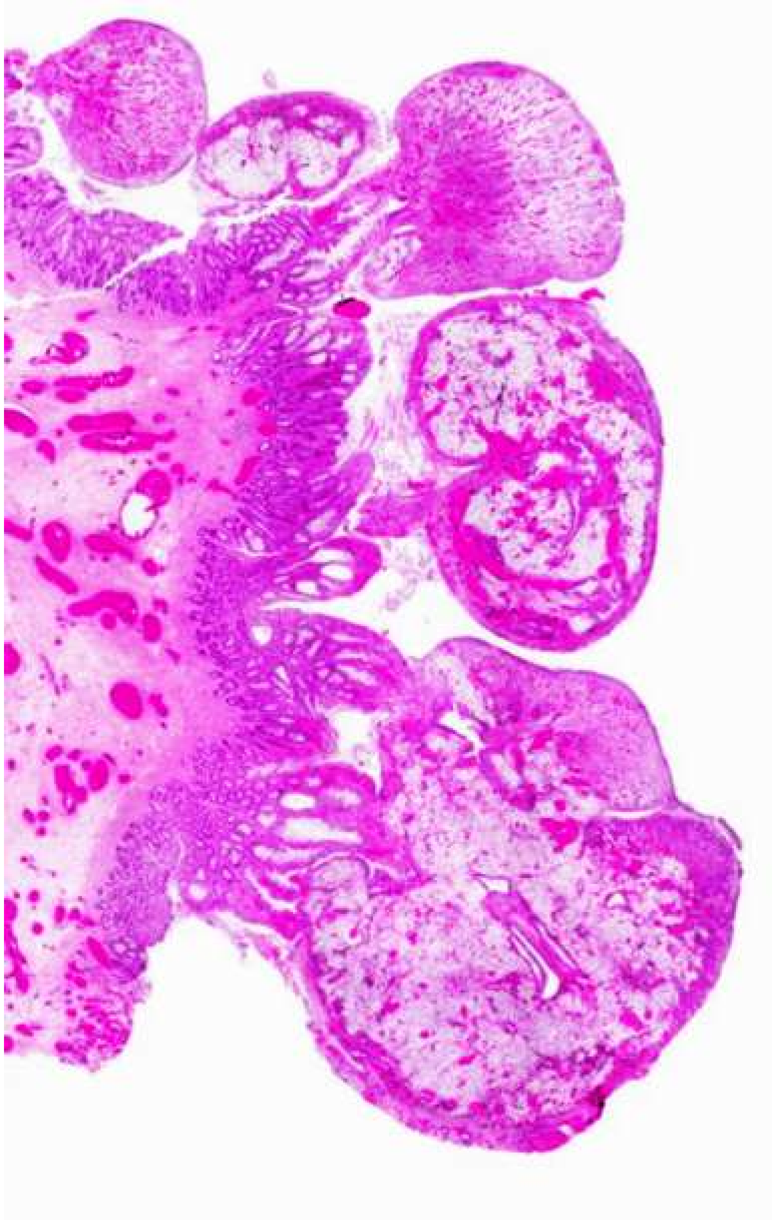




Inflammatory cap polyposis







Mucosal Prolapse Syndrome

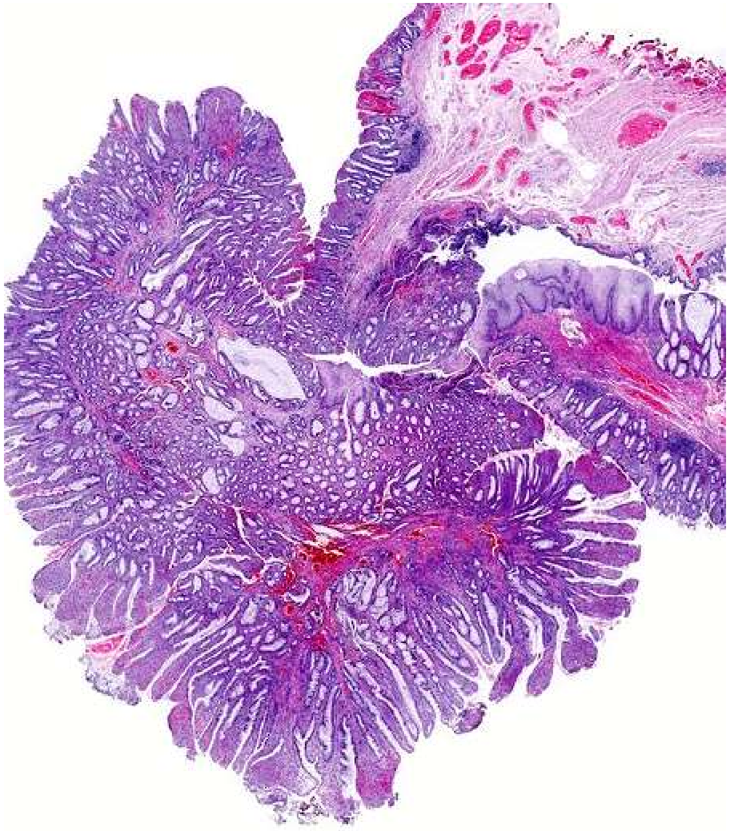
Encompasses a spectrum of conditions related to rectal mucosal prolapse:

- Mucosal prolapse polyp (MPP)
- Solitary rectal ulcer syndrome (SRUS)
- Inflammatory cloacogenic polyps (ICP)
- Inflammatory myoglandular polyp (IMGP)
- Proctitis cystica profunda (PCP)

MPP is a specific type of polyp that results from mucosal prolapse which can be single or multiple and mimic other types of polyps on endoscopy

Both SRUS and MPPs show characteristic histological (fibromuscular proliferation and distortion of the rectal crypts)

SRUS often starts as **rectal erosion or ulcer** (flat and erythematous), which becomes **polypoid**



SRUS and MPP

Closely related and part of a broader condition called **mucosal prolapse syndrome**

SRUS and MPP result from **chronic straining and mucosal prolapse**, leading to various changes in the rectal mucosa

SRUS can present as **ulcers, polyps, or other changes**, while **MPPs present as polyps following mucosal prolapse**

Both conditions share **similar symptoms and microscopic features**

Solitary rectal ulcer syndrome (SRUS)

Rectal bleeding, mucus discharge and an inflammatory lesion of the **anterior rectal wall**

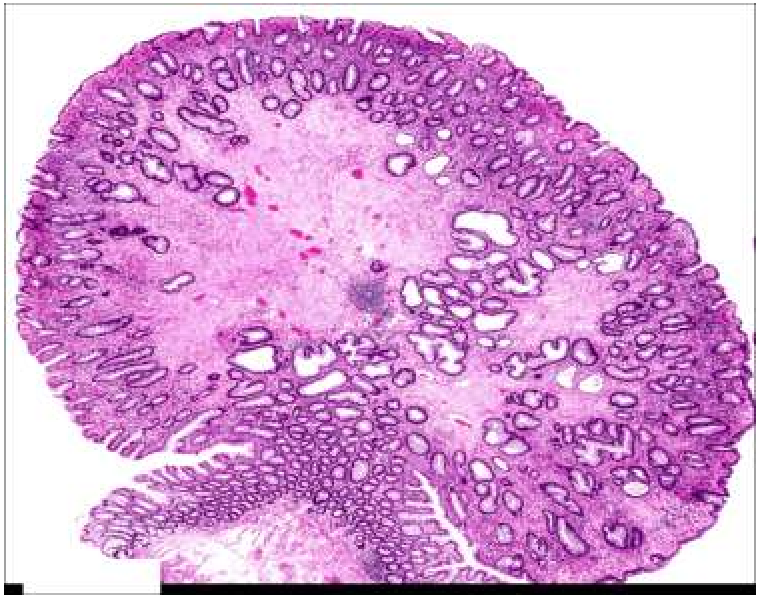
Cause by **impaired relaxation of the anorectal sphincter** that creates a sharp angle at the anterior rectal shelf and leads to **recurrent abrasion and ulceration** of the overlying rectal mucosa

An inflammatory polyp may ultimately form as a result of **chronic cycles of injury and healing**

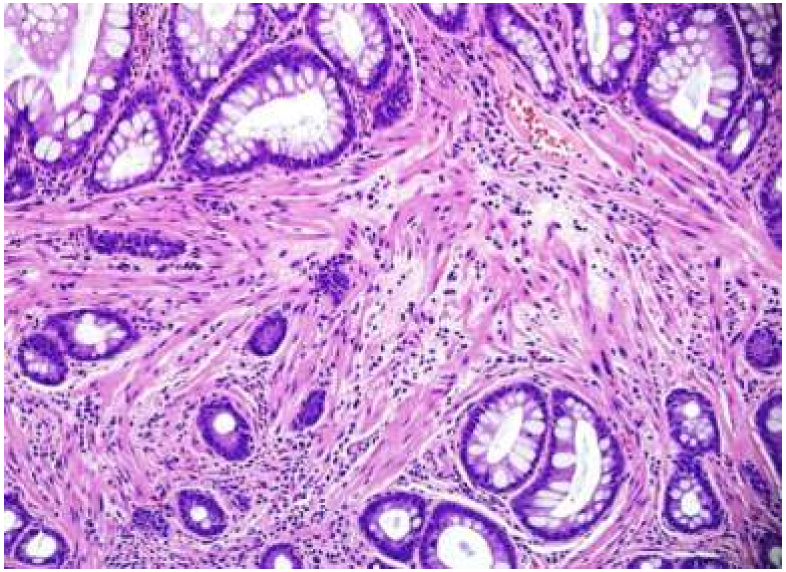
Histological features include **mixed inflammatory infiltrates, erosion, and epithelial hyperplasia** together with prolapse-induced lamina propria **fibromuscular proliferation**

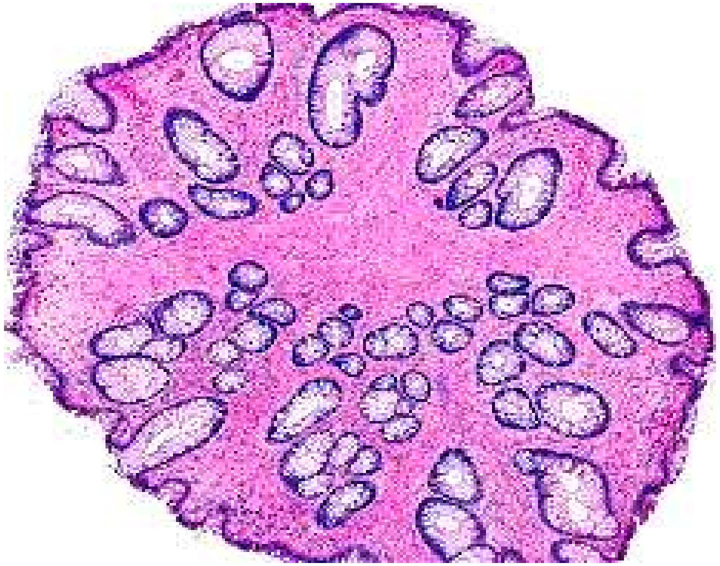
SRUS is a specific condition within the broader category of mucosal prolapse syndrome

Mucosal prolapse polyps are a type of polyp that can occur within this context

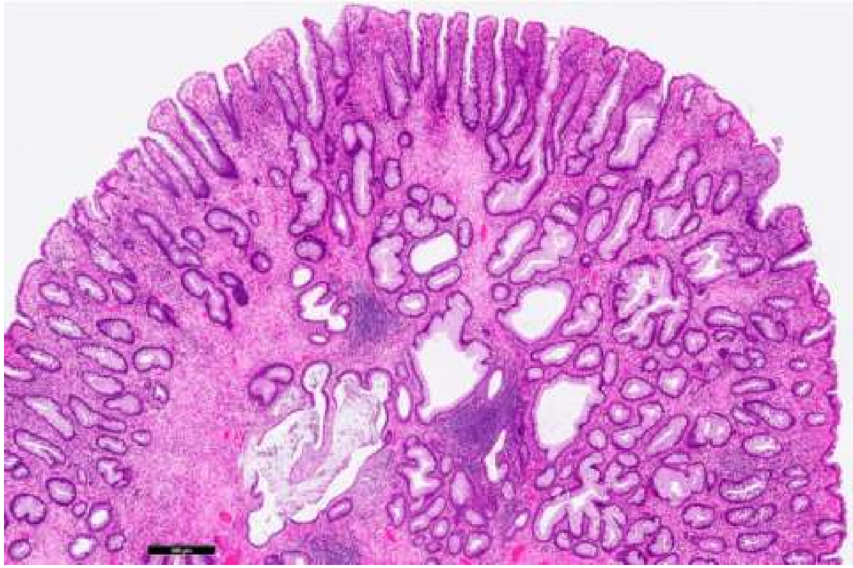


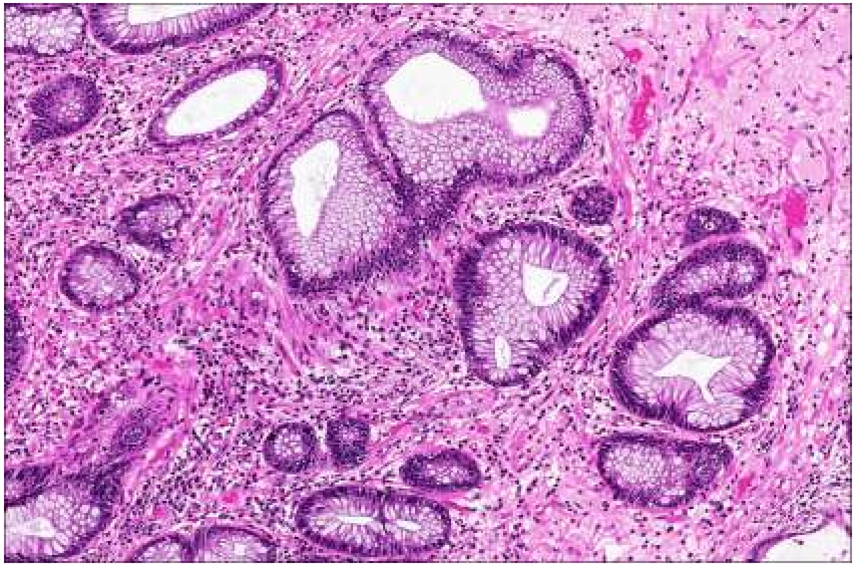
Solitary rectal ulcer syndrome





Solitary rectal ulcer syndrome (SRUS)





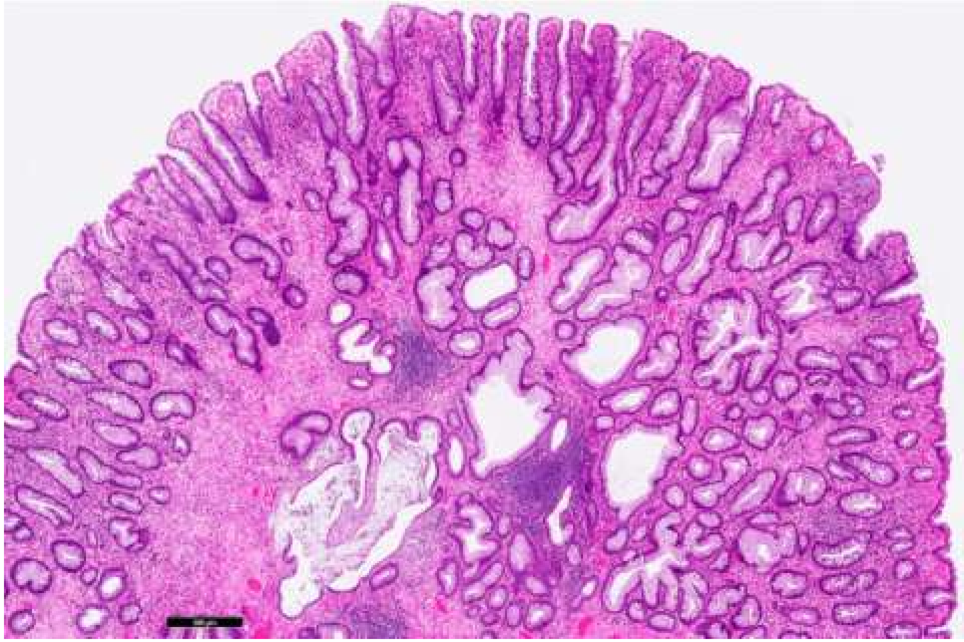
Mucosal prolapse polyps (MPP)

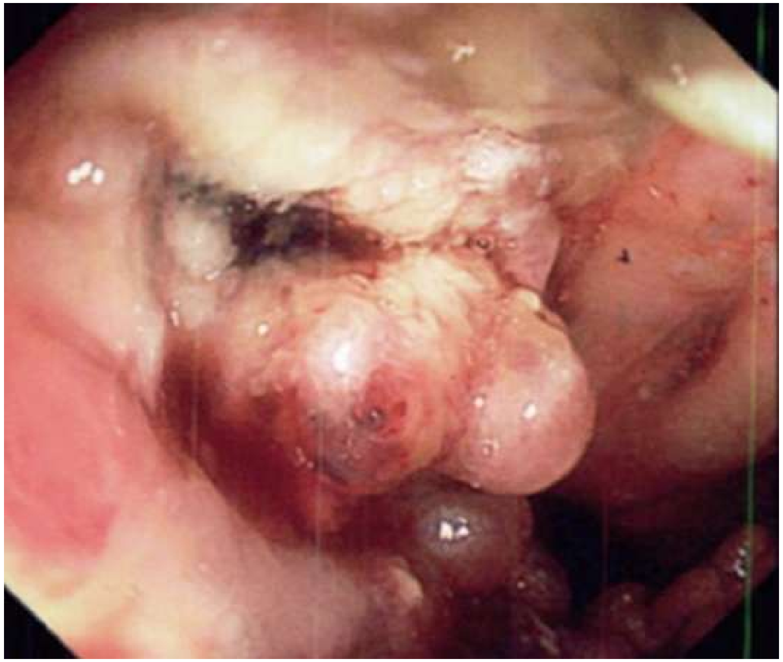
Patchy inflammation, ulcers, polyp formation or stenosis **mimicking malignancy**

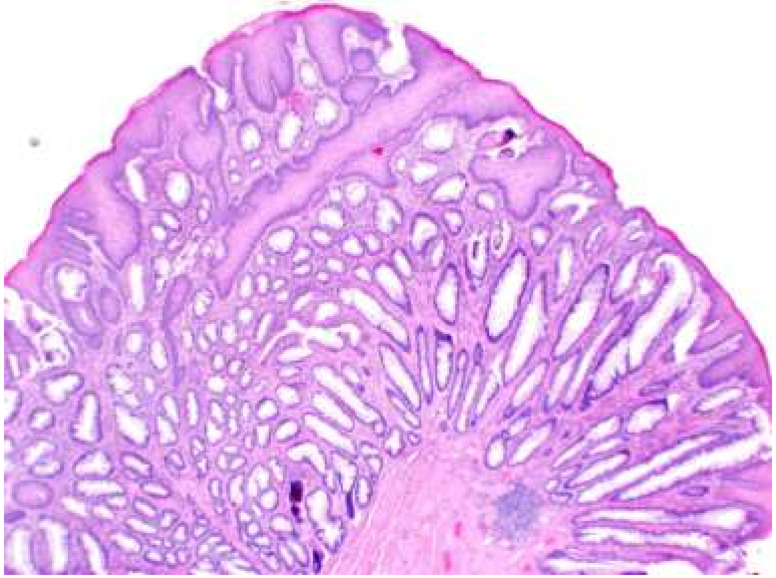
Most commonly found on the **anterolateral rectal wall**

Mucosal erosions and fibrin deposits are accompanied by **hyperplastic and often serrated crypts epithelium** with regenerative epithelial cell changes

Smooth muscle extension into the mucosa and surround the crypts







Inflammatory cloacogenic polyp (ICP)

Non-neoplastic polyp

Arises in the **anal transitional zone**

Inflammation and glandular and smooth muscle proliferation

Related to a **low-fiber diet** (increase intraluminal colonic pressure)

Similar to mucosal prolapse syndrome (solitary rectal ulcer syndrome, rectal prolapse and proctitis cystica profunda)

Does not recur after removal

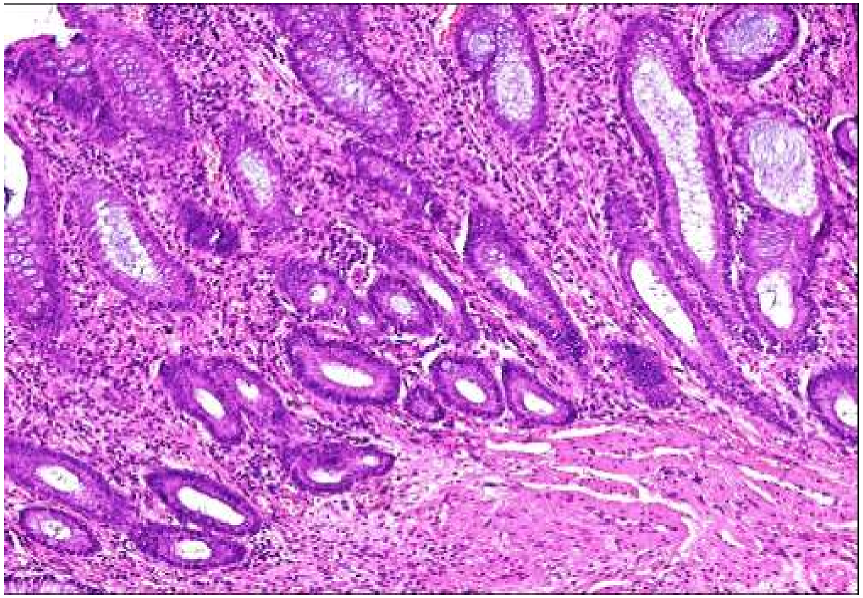
Inflammatory cloacogenic polyp

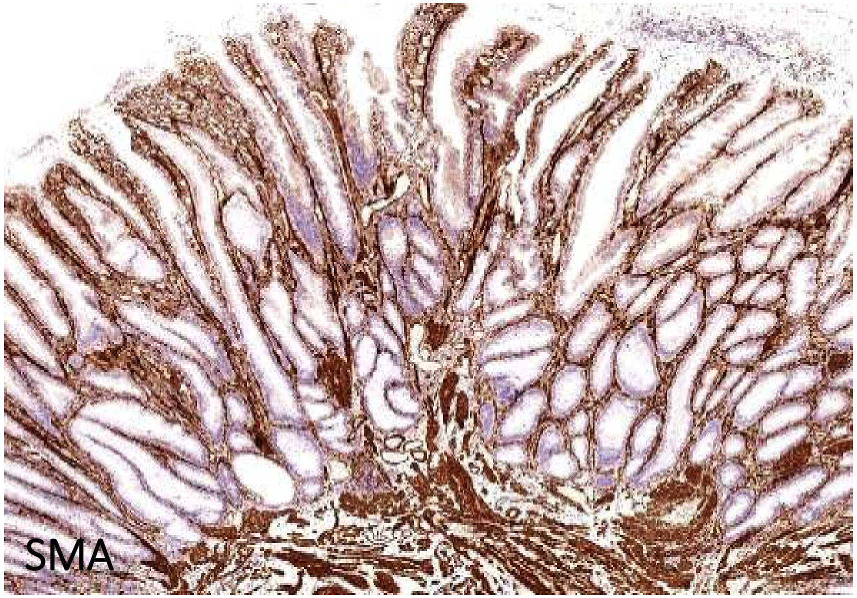
Covered by **hyperplastic epithelium** (squamous, columnar or transitional)

Complex **tubulovillous growth** with cystic change

Active chronic **inflammation, granulation tissue, vascular ectasia and oedema**

Fibromuscular proliferation and obliteration of the lamina propria in a radial fashion





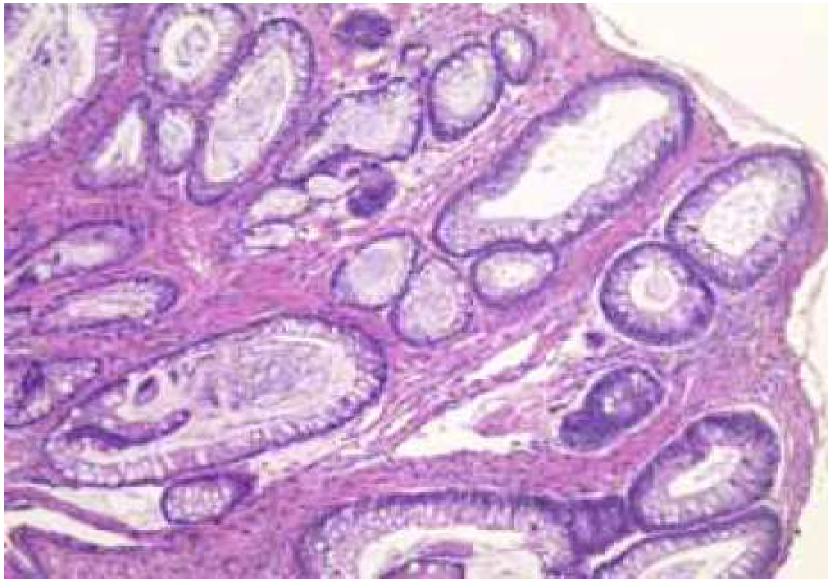
Inflammatory myoglandular polyp (IMGP)

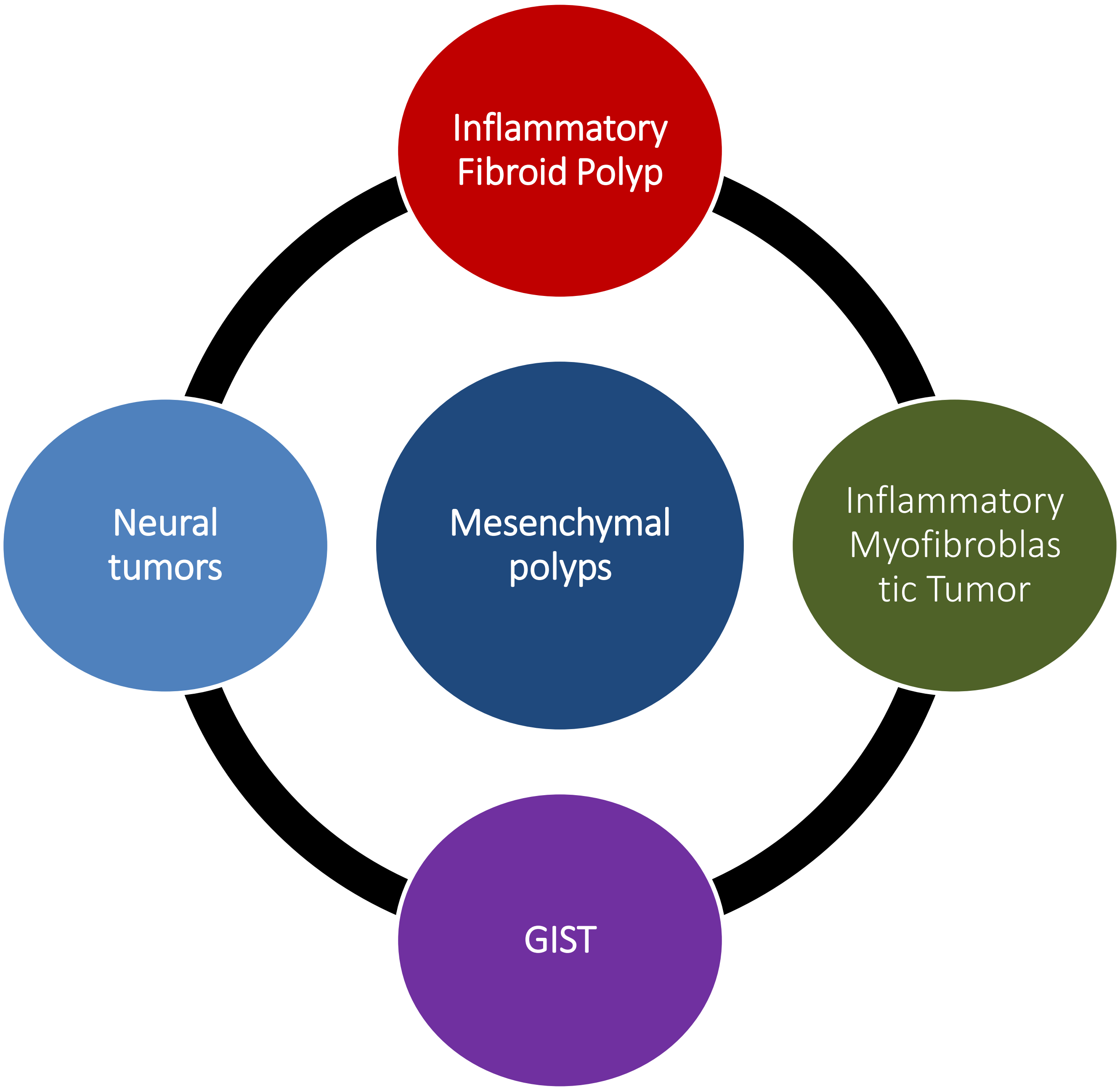
Non-neoplastic polyp of unclear etiology, commonly located in **colon and rectum**

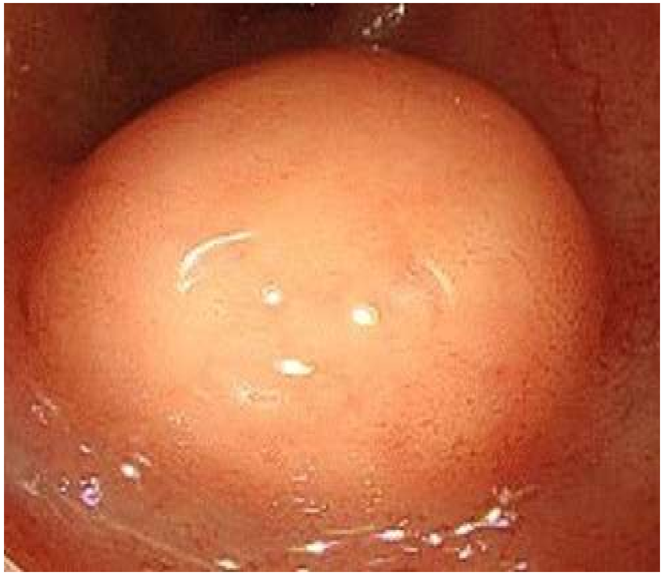
Smooth surface, pale color, **inflammatory granulation tissue**, **smooth muscle proliferation** and **hyperplastic glands with cystic changes**

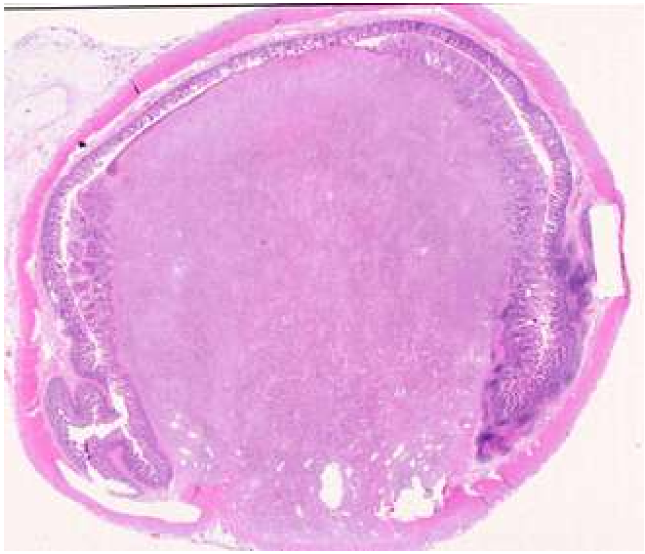
Can be **aymptomatic** or cause symptoms like **rectal bleeding**, positive fecal occult blood test and **iron deficiency anemia**

Etiology is unclear but **chronic trauma** from the fecal stream and peristalsis may play a role




Inflammatory Fibroid Polyp
Neural tumors
Mesenchymal polyps
Inflammatory Myofibroblastic Tumor
GIST





Inflammatory Fibroid Polyp (IFP)

Generally **sporadic**

Multiple IFPs can develop in patients with **germline PDGFRα mutations**

Stomach and ileum are most often affected

Rare in colorectum or other sites in the GI

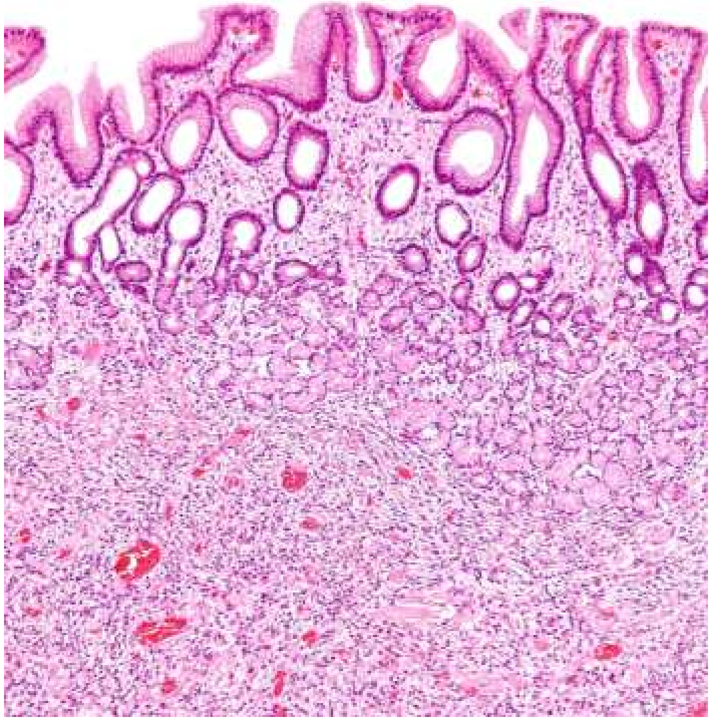
Tumors is **centered in the submucosa**

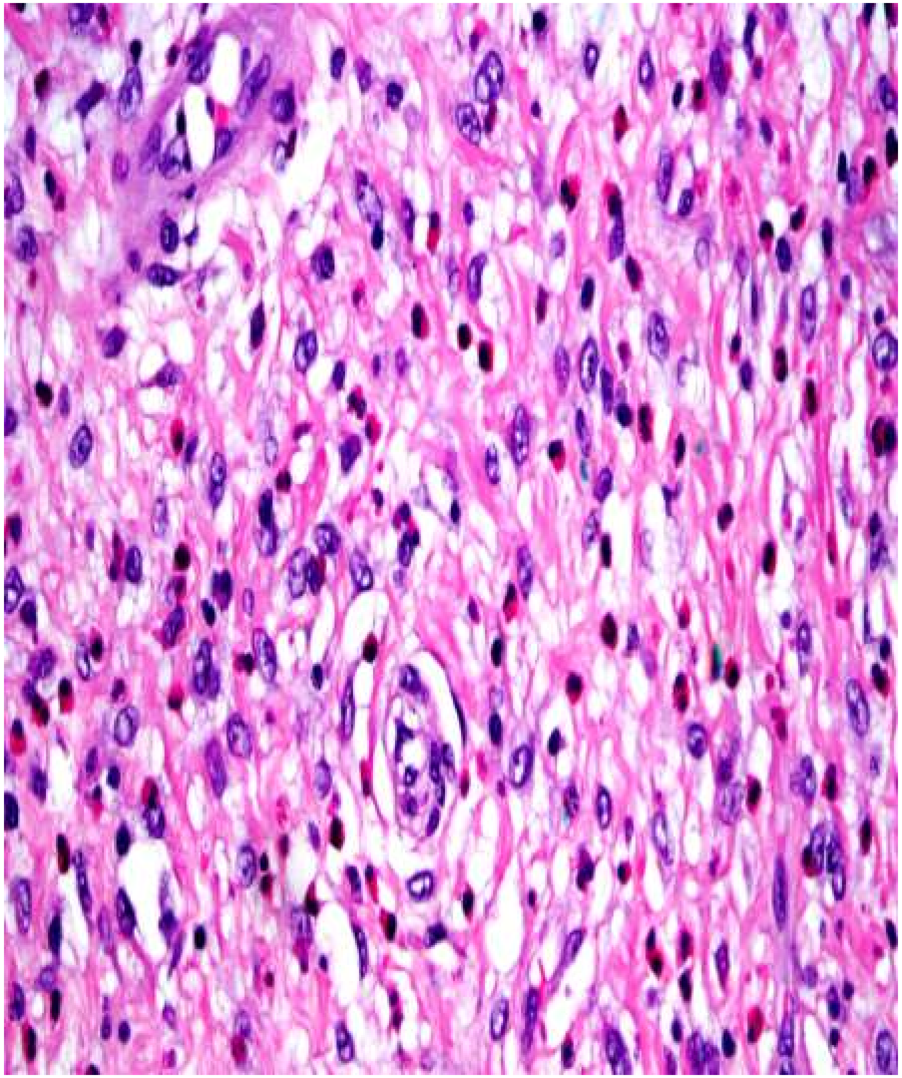
Disorderly proliferation of **bland spindle cell** in **loose stroma** containing numerous eosinophils and scattered mononuclear cells

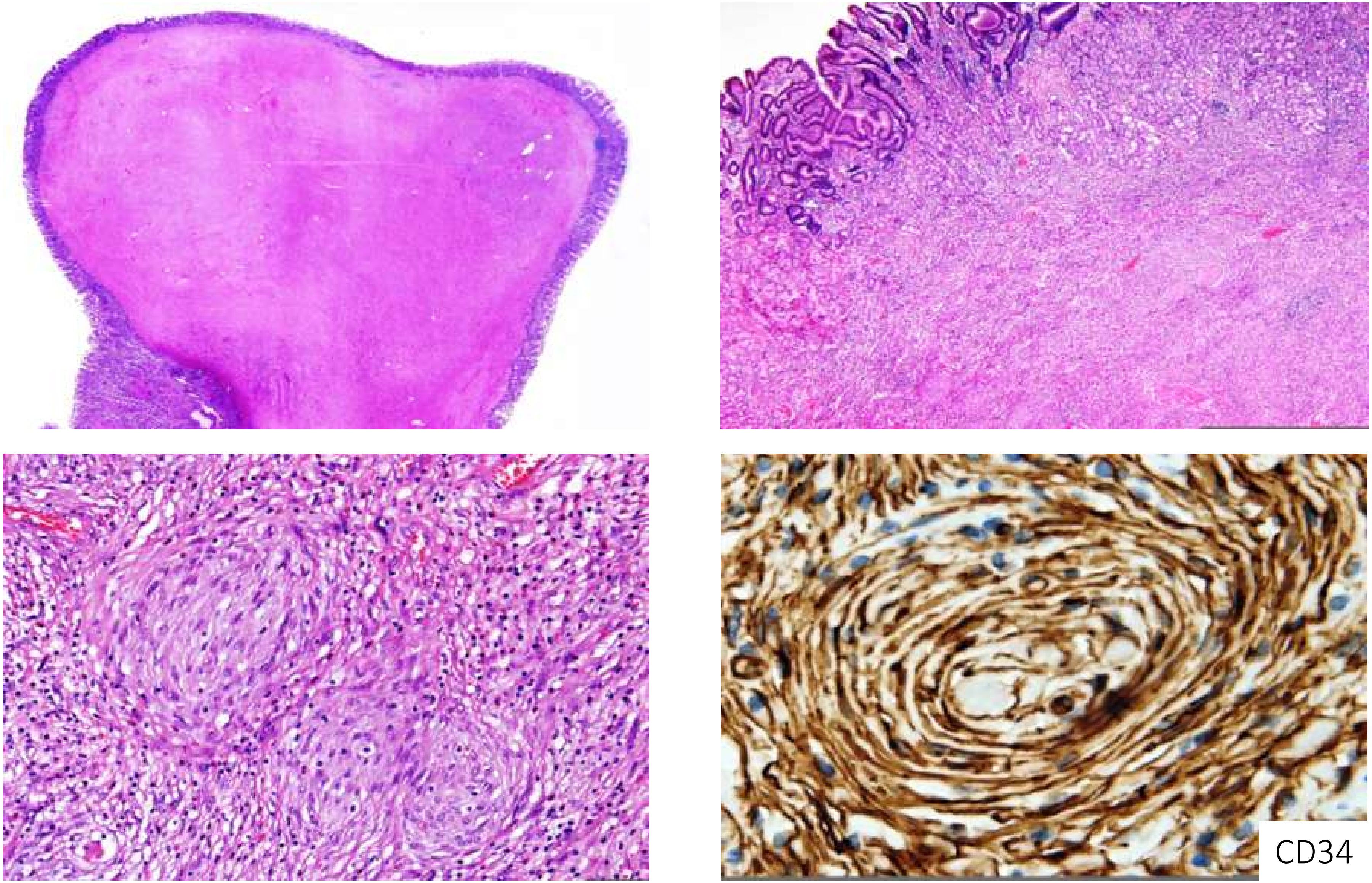
Stromal spindled cells are **vimentin, actins and CD34 positive but CD117 negative**

Scattered CD117-positive **mast cells** are frequently present

Inflammatory Fibroid Polyp (IFP)







Inflammatory Fibroid Polyp (IFP)

Inflammatory Myofibroblastic Tumor (IMT)

Myofibroblastic neoplasm of borderline malignancy

High **recurrence rate but low metastatic potential**

Composed of fibroblasts, myofibroblasts, lymphocytes, plasma cells, eosinophils, and histiocytes

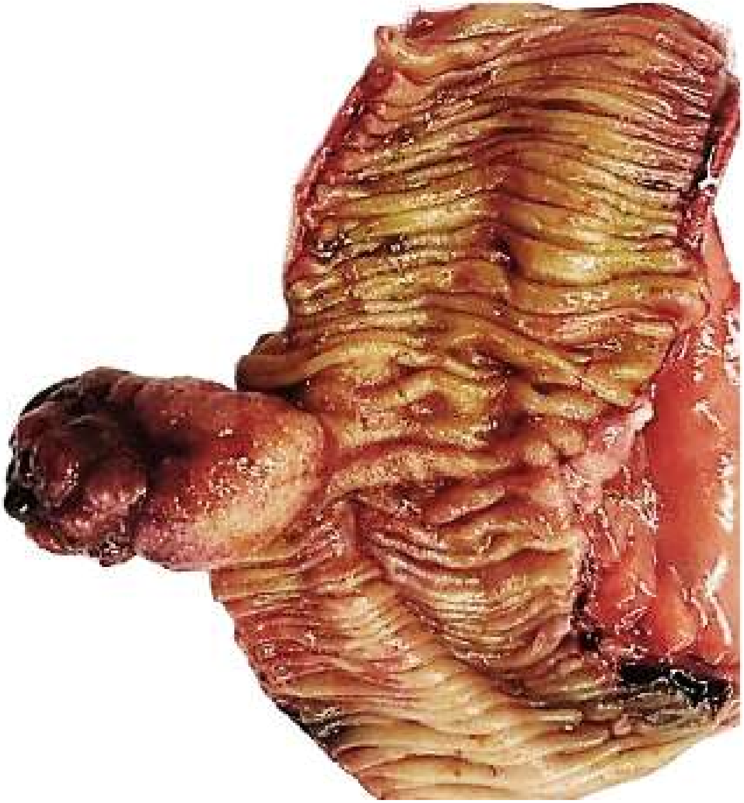
Lungs, GI tract, female genital tract, bladder, mesentery and omentum

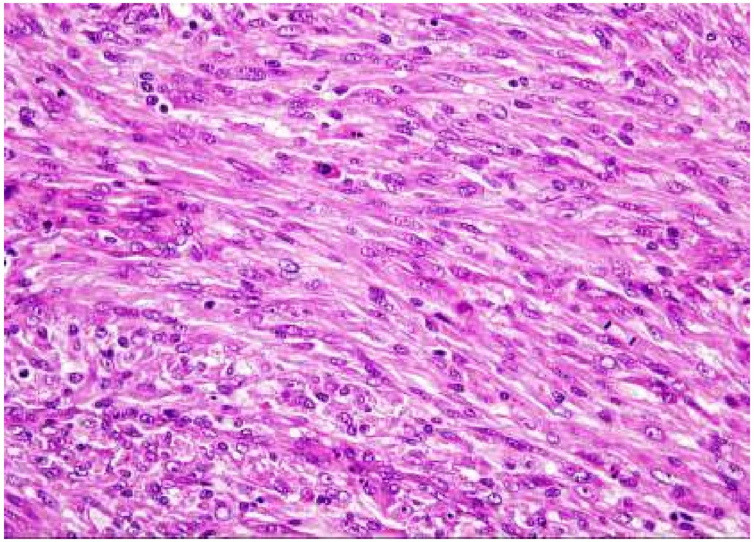
Predilection for **young adults**

Mass effect and systemic symptoms (fever, leukocytosis, anemia, hypergammaglobulinemia)

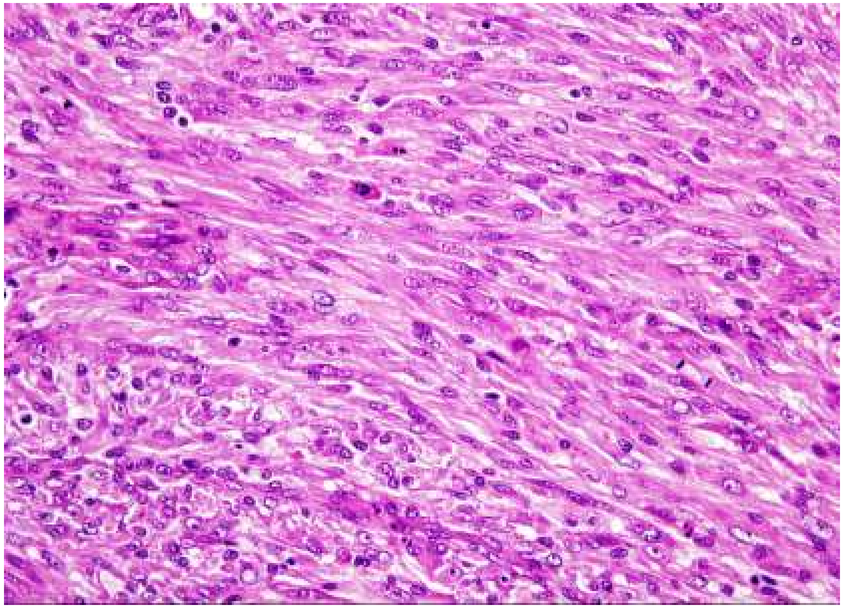
Two-thirds have **TK receptor gene rearrangements**, involving **ALK** 2p23

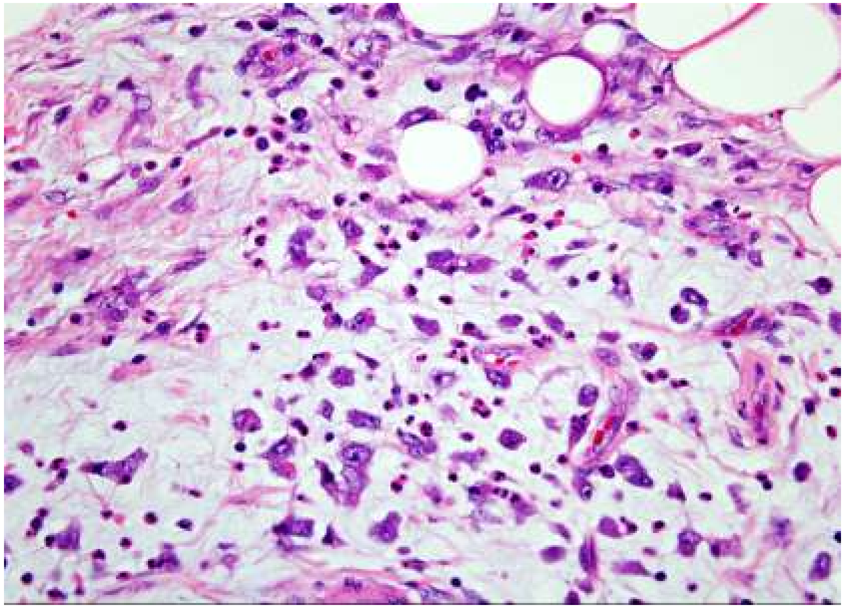
Other mutations (ROS1, NTRAK3, PDGFB and RET) can also be seen

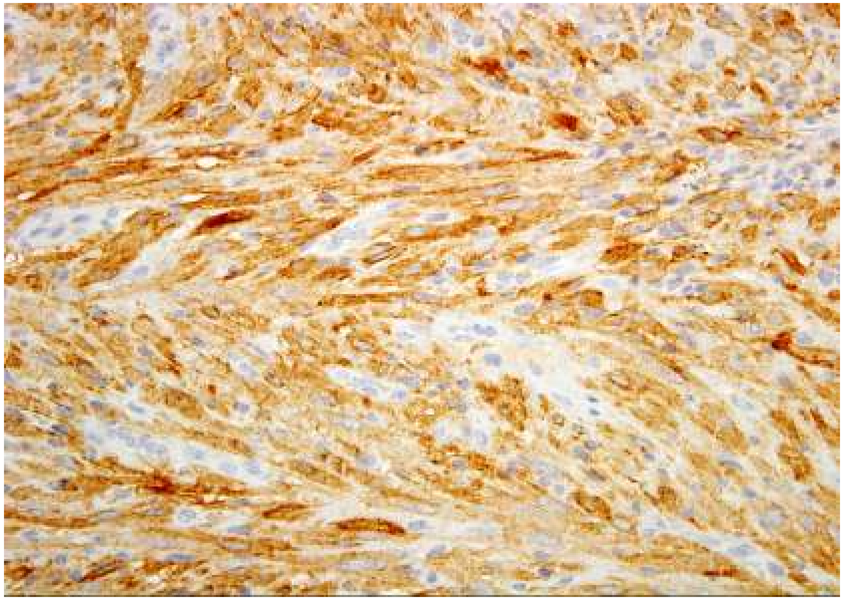




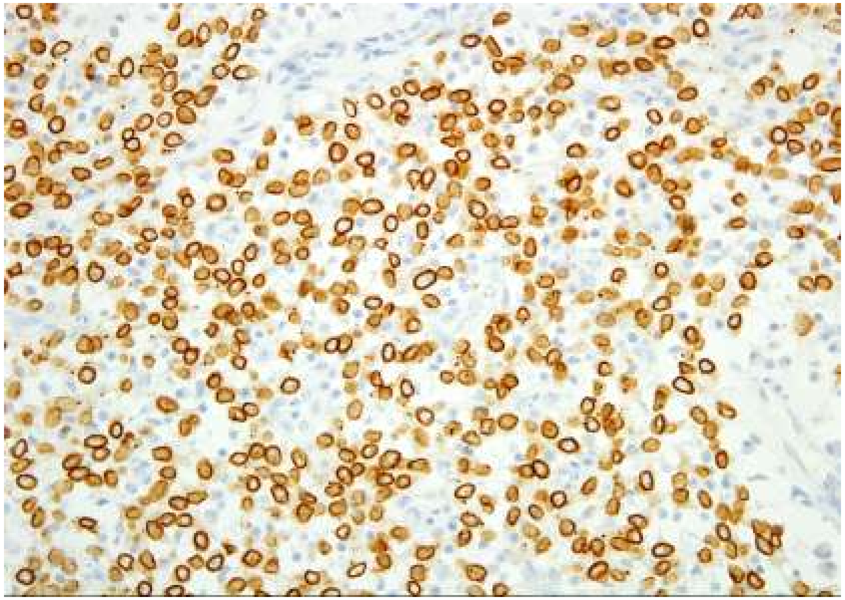
Inflammatory myofibroblastic tumor (IMT)



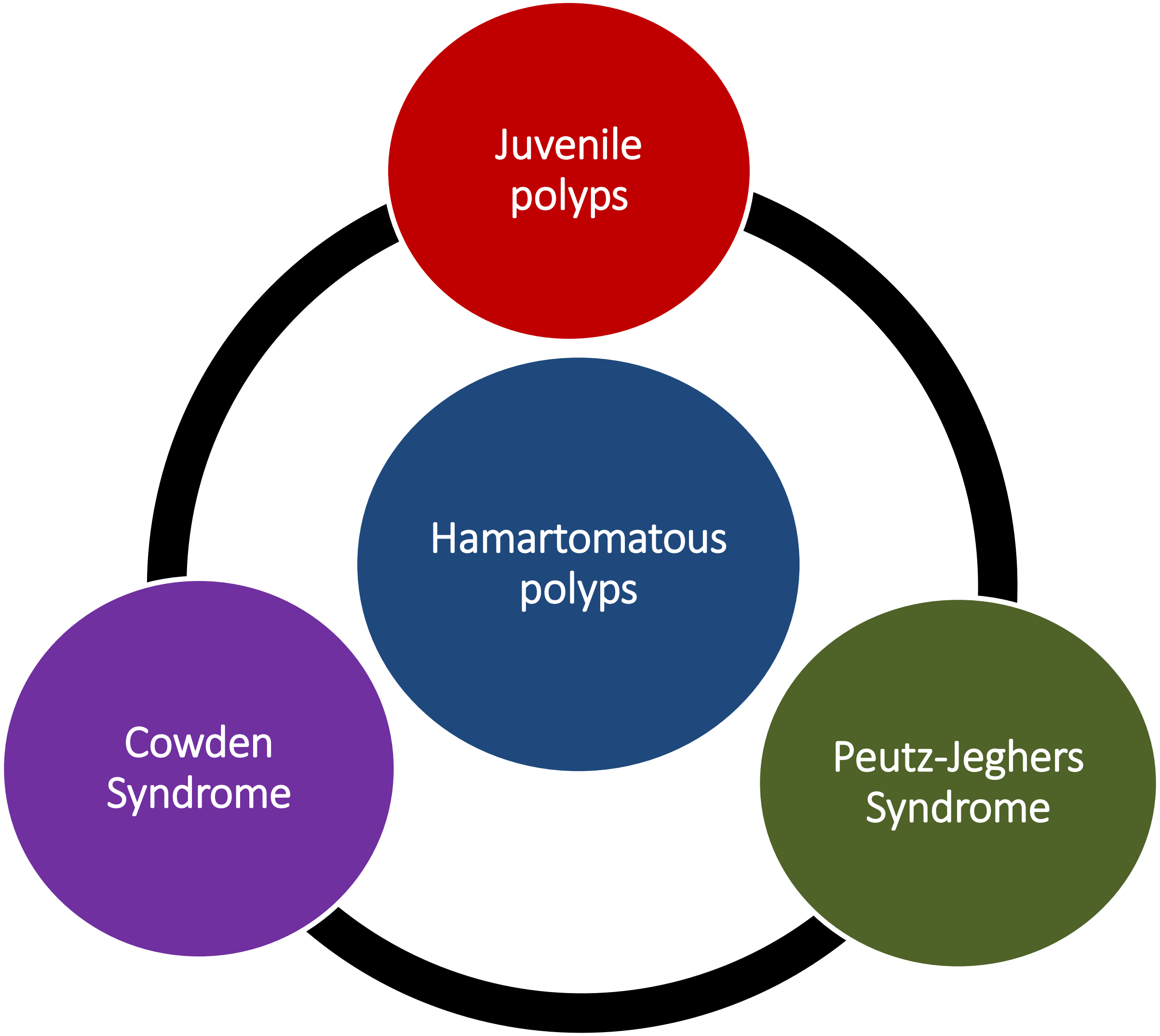




ALK



ALK



Hamartoma is abnormal collection of normal tissues native to the site (benign mass of disorganized normal tissue)

Hamartomatous polyps

Hamartoma is **abnormal mixture of tissues** normally found at that site

Mostly **developmental abnormalities**, some are caused by germline **mutations** in tumor suppressor genes or proto-oncogenes

Some are associated with increased **cancer risk**, either within the polyps or at other intestinal or extraintestinal sites

A subset can be considered to be **premalignant** (neoplastic lesions, much like adenomas)

Associated **extra-intestinal manifestations**

Other family members may be affected

Juvenile Polyps

Hamartomatous polyps (focal malformations of the mucosa)

Can be **sporadic or syndromic**

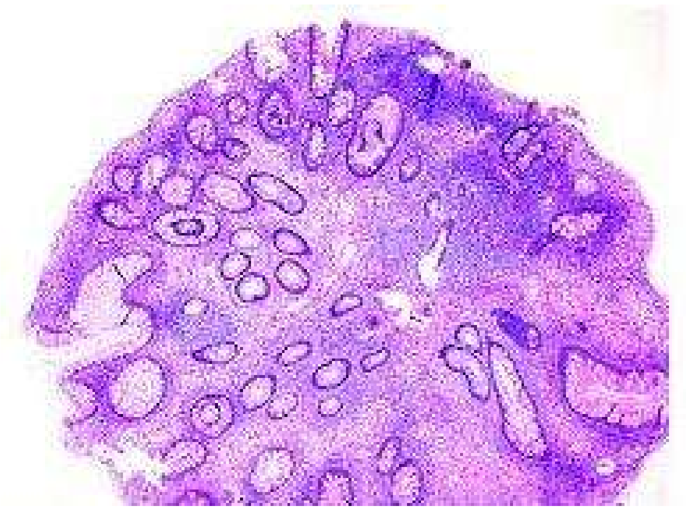
Sporadic juvenile polyps are referred to as **retention polyps**

Majority occur in **children** younger than 5 years of age but can be seen in older ages

Commonly seen in the **rectum** and cause **bleeding**

May cause **intussusception, intestinal obstruction prolapse**

Can be associated with **polyps in other parts of the GI** and extra GI congenital **malformations**



Can be large up to <30 mm in diameter

Typically **pedunculated, smooth-surfaced, reddish lesions** with characteristic **cystic spaces**

Microscopically **cystically dilated glands** filled with **mucin** and **inflammatory debris** seen

Remainder of the polyp is composed of **lamina propria expanded by mixed inflammatory infiltrates**

Muscularis mucosae may be normal or attenuated

Juvenile polyposis syndrome

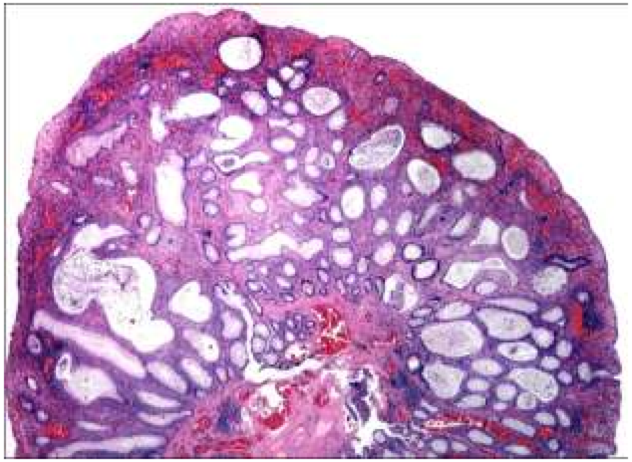
Rare autosomal **dominant syndrome**

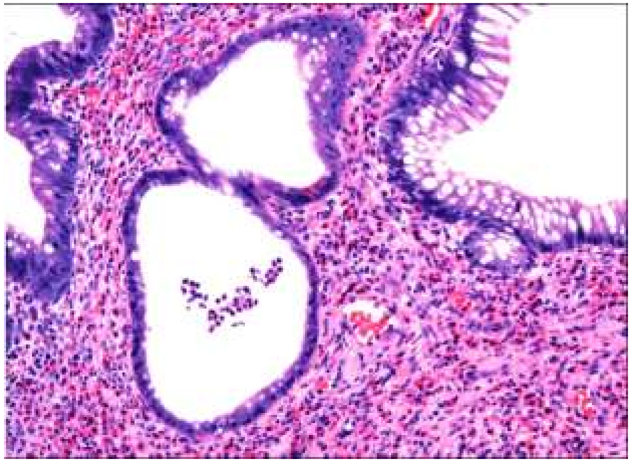
- **5 or more juvenile polyps in the colorectum**
- **Juvenile polyps throughout the GI**
- **Any number of juvenile polyps and a positive family history of juvenile polyposis**

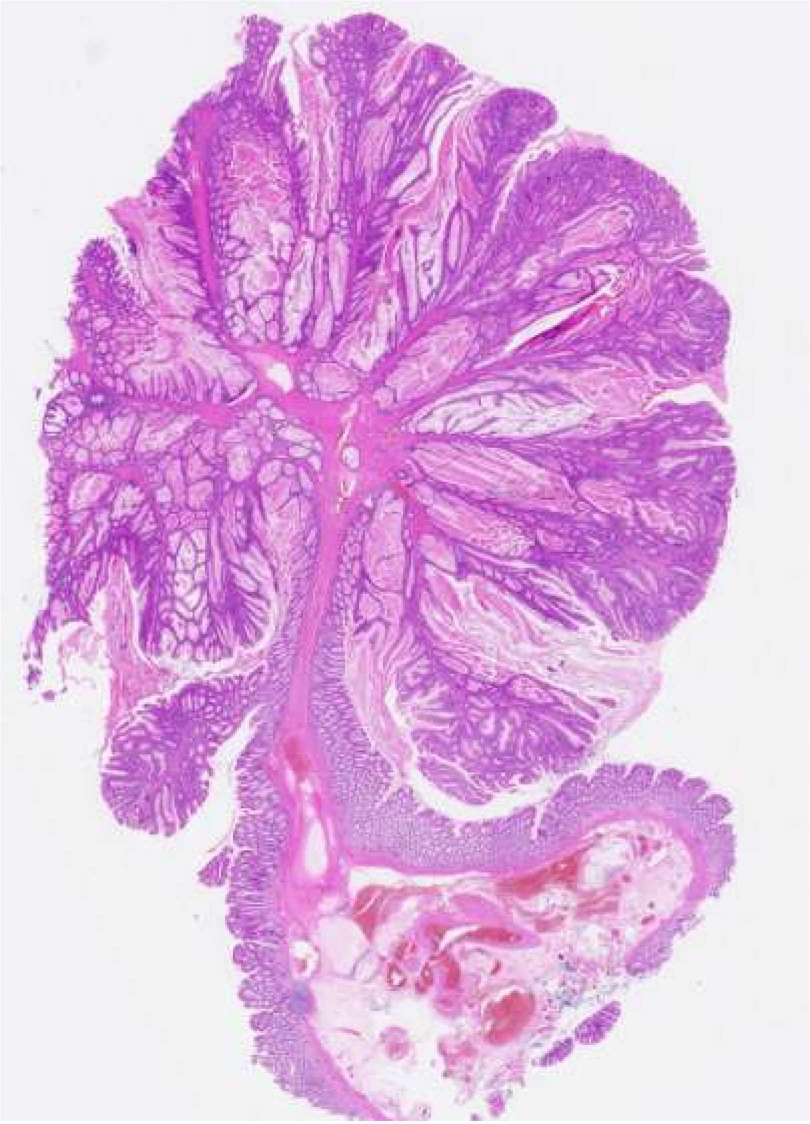
Increased risk of colorectal cancer with cumulative life-time risk of colorectal cancer is 40% and the relative risk is 34

Edematous lamina propria with inflammatory cells and cystically dilated glands lined by cuboidal to columnar epithelium with reactive changes

Germline mutation in the SMAD4 or BMPR1A gene is found in at least 50%







Peutz-Jeghers polyps with lobular crypt organization and smooth muscle arborizing proliferation

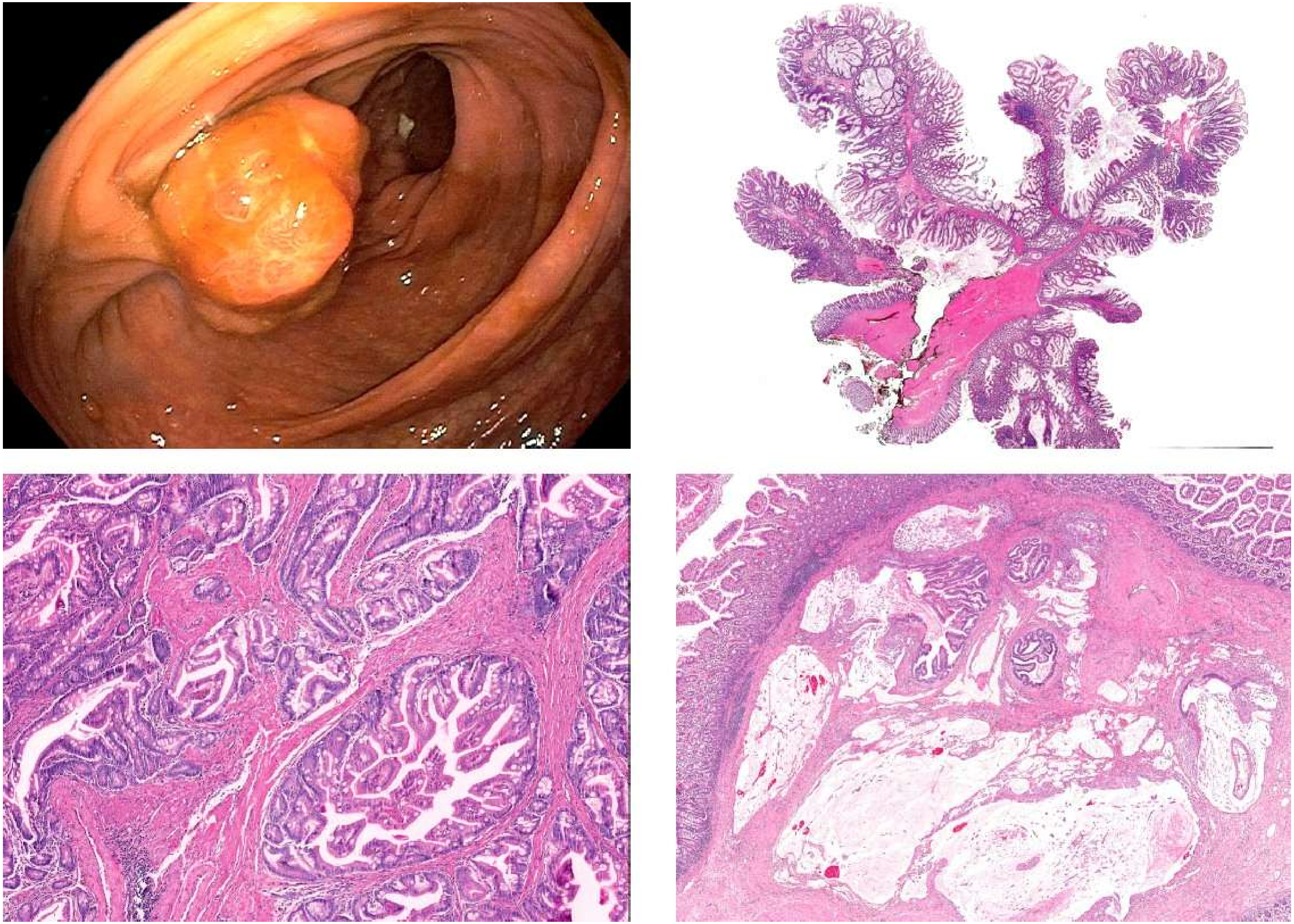
Peutz-Jeghers syndrome (PJS)

GI polyposis and mucocutaneous pigmented macules

STK11 gene mutations

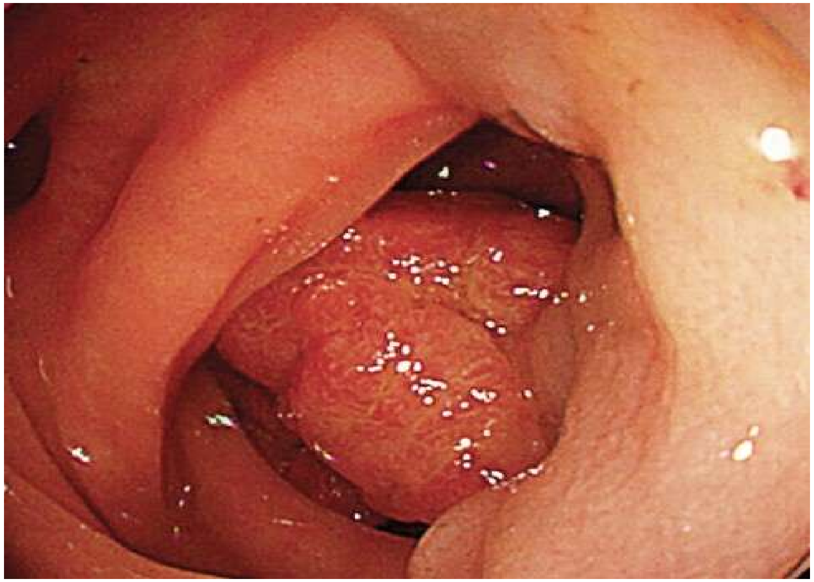
Increased risk of cancer development in the GI (colorectal, pancreatic and gastric) and non-GI (breast, uterine, cervical, lung, ovarian and testicular)

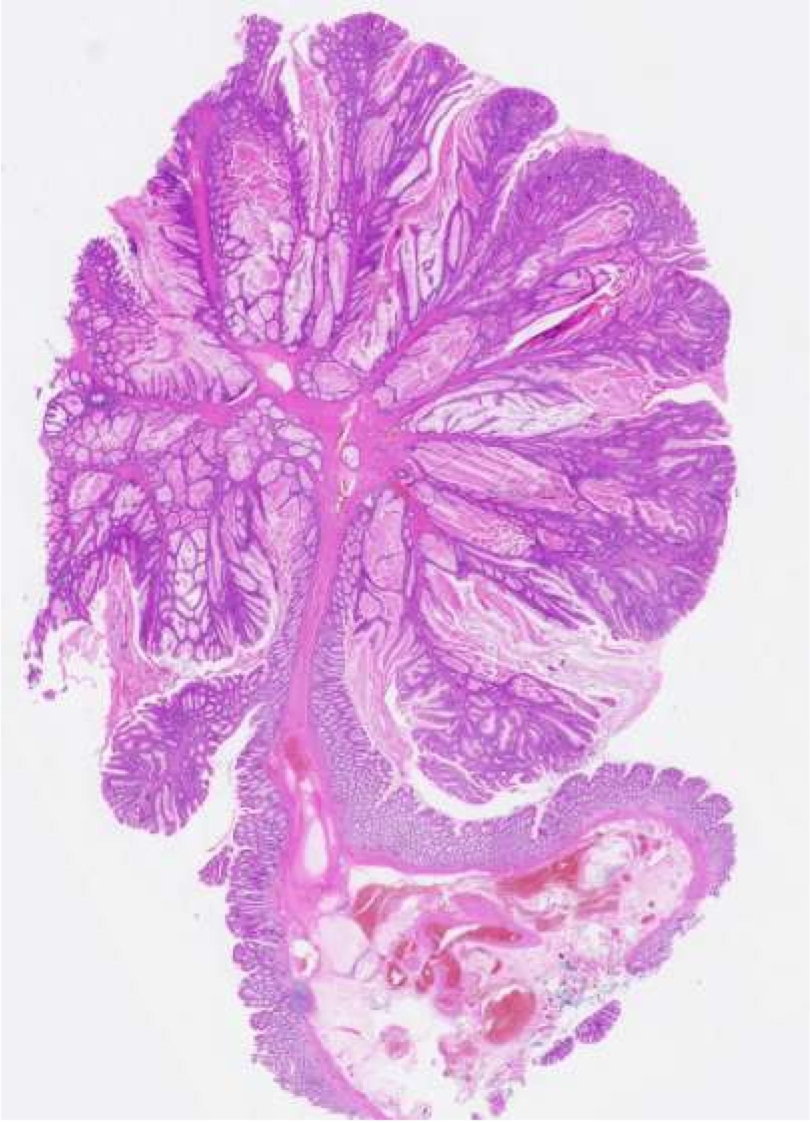
Colorectal cancer is most common with a lifetime risk of 39%, followed by **breast cancer** in females (35%)



Peutz-Jeghers syndrome

Peutz-Jeghers syndrome (PJS)





Cowden syndrome

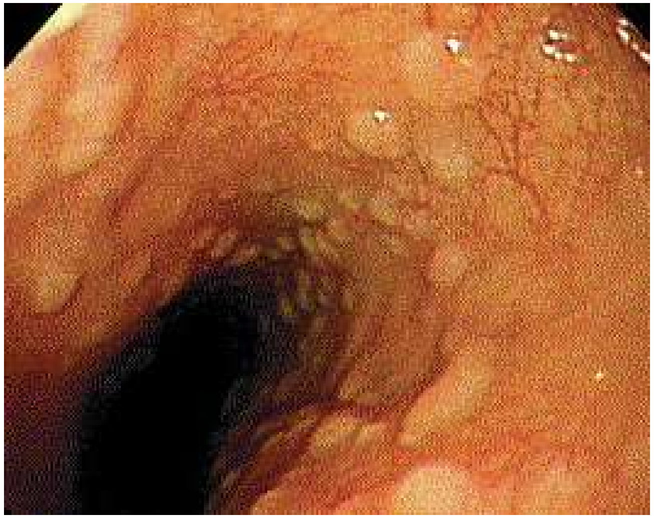
Autosomal dominant genodermatosis

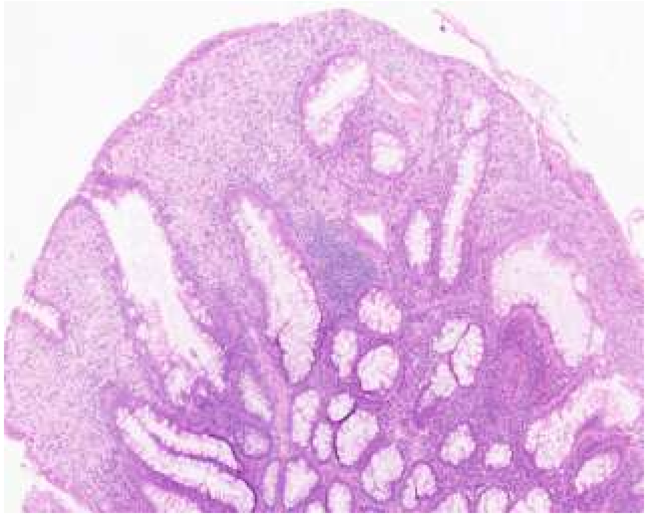
With mutations in the tumor suppressor gene Phosphatase and Tensin homolog gene **(PTEN)**

Spectrum of polyps includes **hamartomatous, inflammatory, adenomatous, ganglioneuromatous, hyperplastic and juvenile polyps**

Mucocutaneous lesions and macrocephaly

Malignant neoplasm of the thyroid, endometrium or breast





Cronkhite-Canada syndrome (CCS)

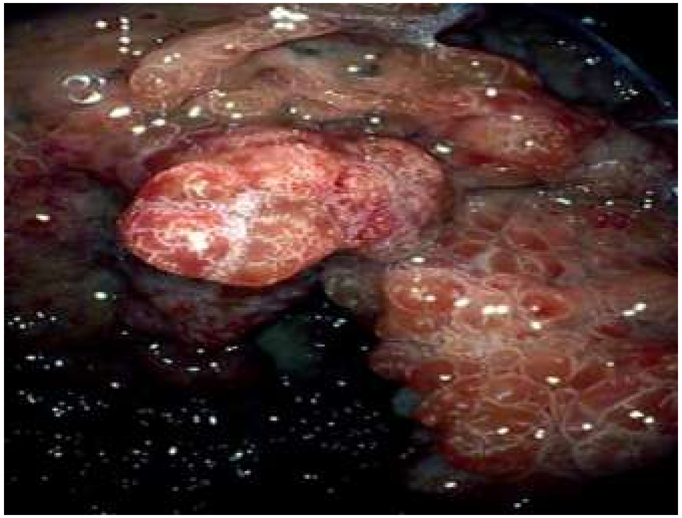
Non-hereditary condition

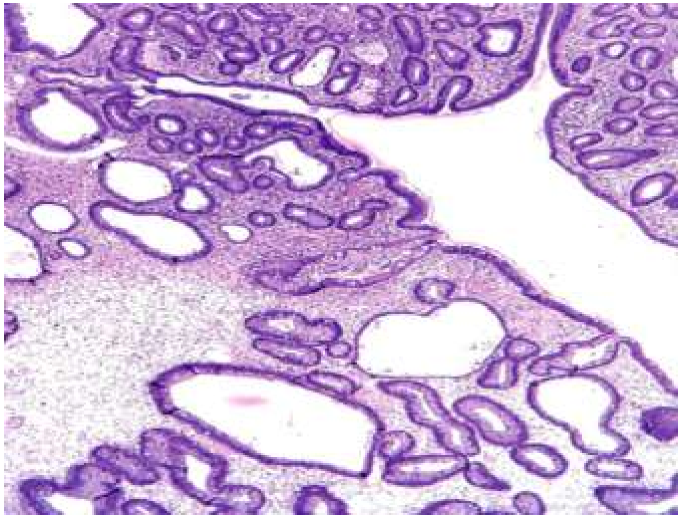
GI hamartomatous polyps
Diarrhea
Dermatological triad (hyperpigmentation, alopecia and onychodystrophy)

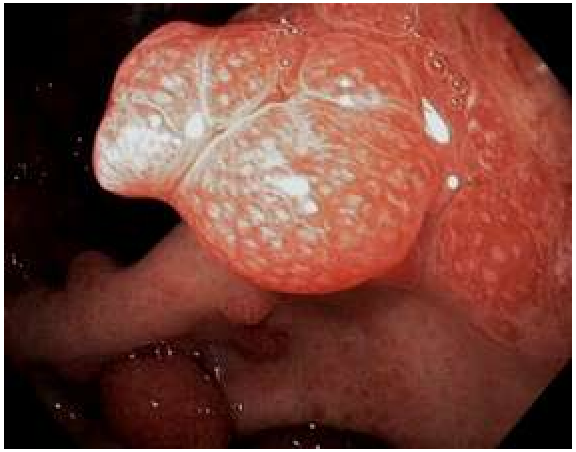
Etiology is unknown

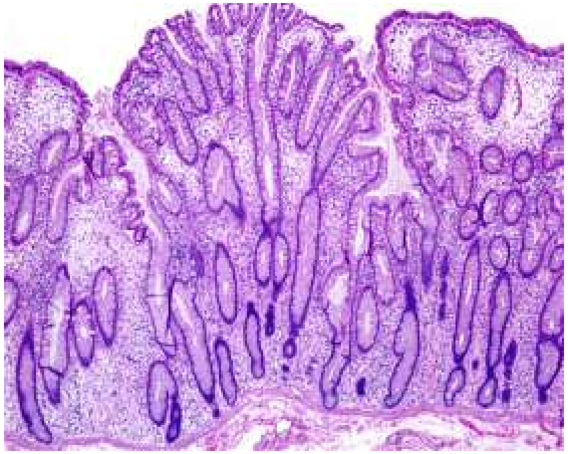
Multiple polyps that can be **found throughout the GI**

Markedly expanded **edematous lamina propria with inflammation and cystic glandular transformation**, often resembling a **juvenile polyp**









Cronkhite-Canada syndrome (CCS)

Multiple sessile polyps throughout the GIT

Cystic dilatation of crypts

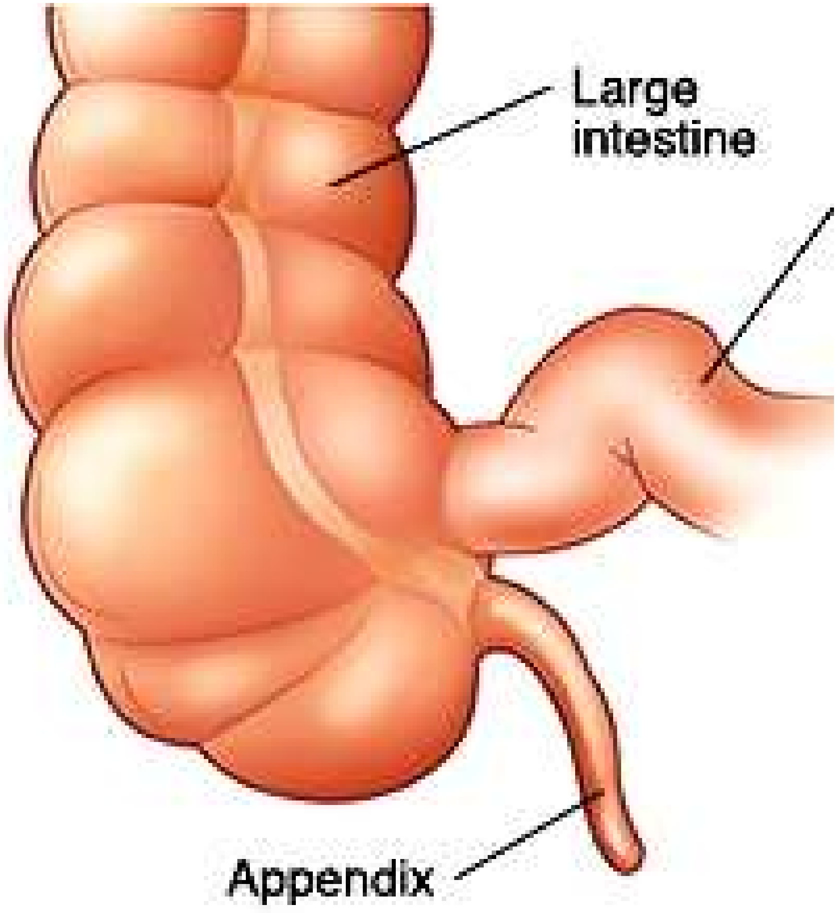
Lamina propria edema and inflammation

smooth muscle bundles

No dysplasia

Polyposis syndromes

- **Familial adenomatous polyposis**
  APC gene mutations
- **Juvenile polyposis**
  SMAD4 gene mutations
- **Peutz-Jeghers syndrome**
  STK11 gene mutations
- **Cowden syndrome**
  PTEN gene mutations
- **Cronkhite-Canada syndrome**
  Non-hereditary polyposis
- Other



Appendiceal polyps

Serrated polyps

Adenomas

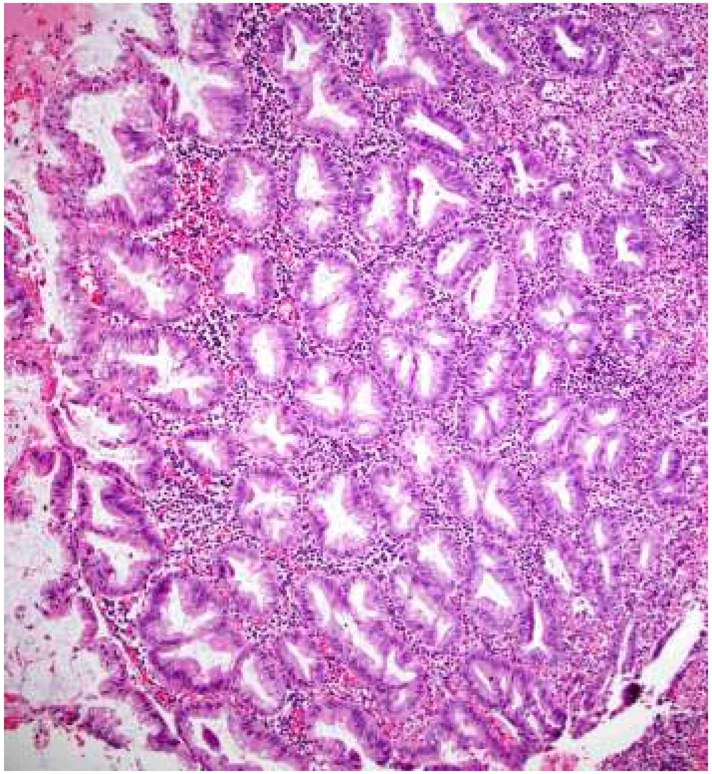
Hyperplastic polyp

Hyperplastic polyps protrude into the lumen but **do not involve the entire appendiceal circumference**

Small, spanning no more than a few millimeters, and resemble microvesicular hyperplastic polyps of the colorectum

Contain both goblet cells and non-goblet mucinous epithelial cells

Unlike microvesicular hyperplastic polyps of the colorectum, appendiceal lesions **infrequently harbor BRAF mutations, but may contain KRAS mutations**

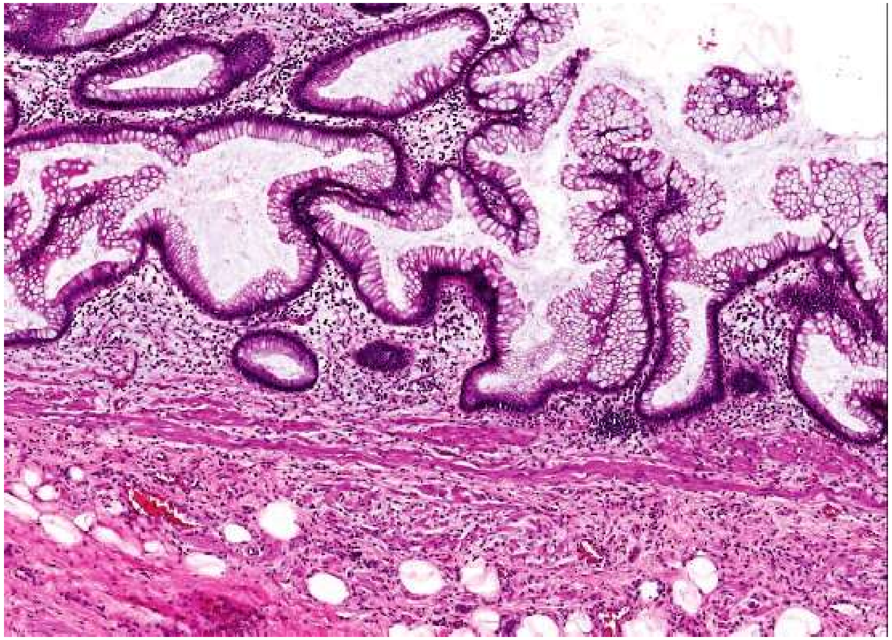


Diffuse mucosal hyperplasia

Common finding in **surgically removed appendectomy specimens**, particularly when patients undergo **delayed appendectomy following appendicitis**

Circumferential proliferation of expanded crypts enriched with goblet cells with slightly serrated architecture

Often seen in combination with **ruptured appendiceal diverticula and organizing appendicitis**



Appendiceal sessile serrated lesion

Occurs in **adults**

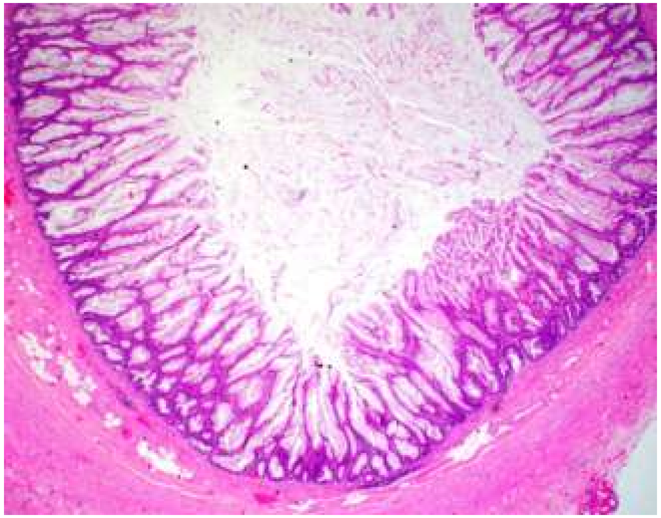
Detected in **appendectomy** or right colectomy specimens

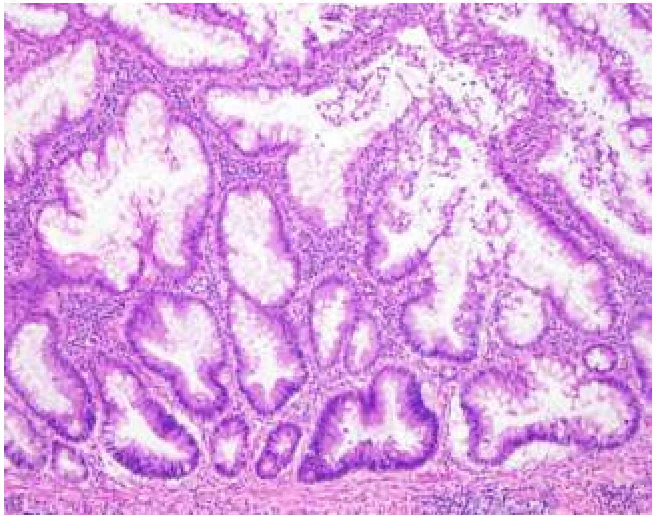
Appendiceal SSLs can occur in **association with carcinomas of the right colon or serrated polyposis**

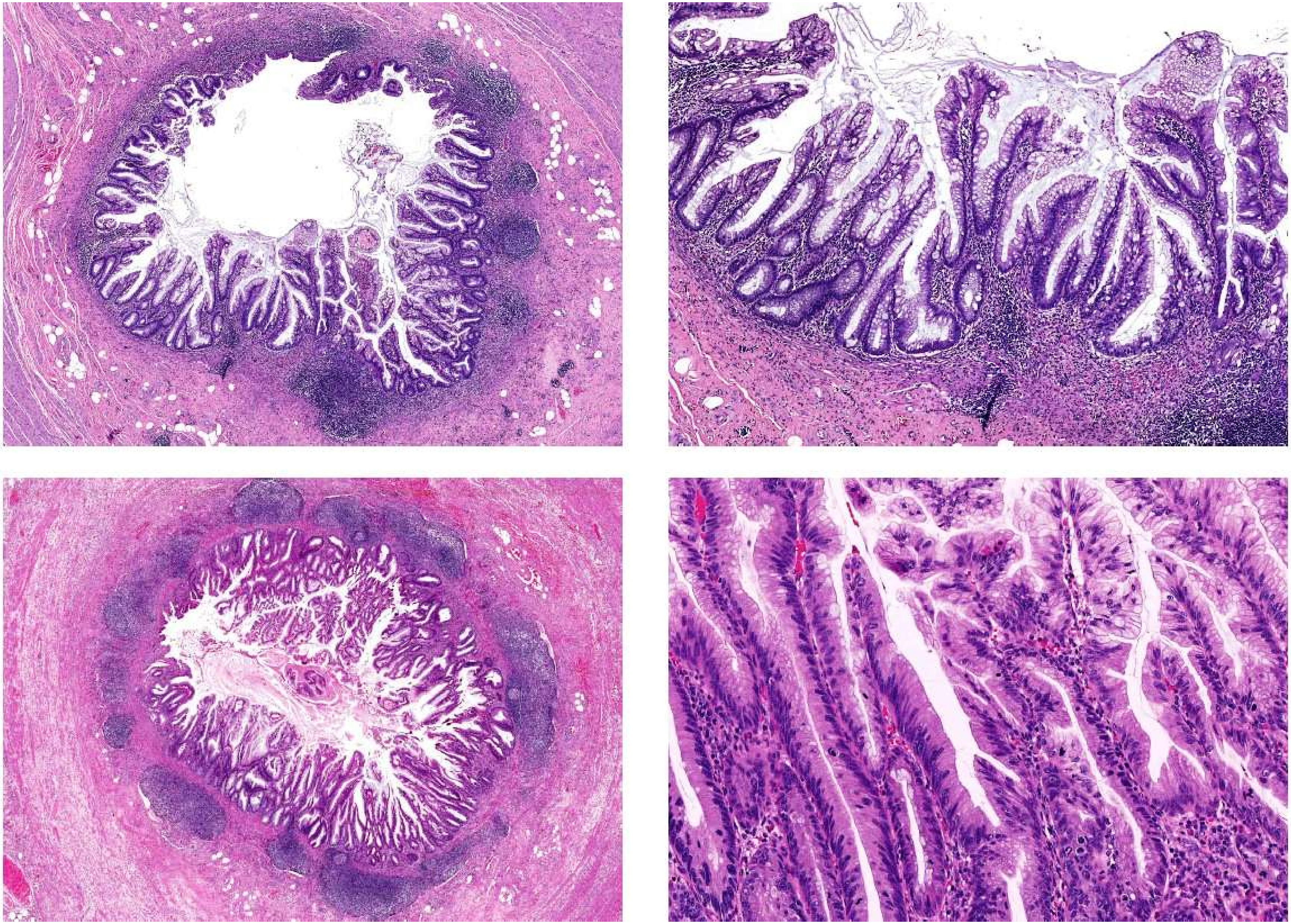
Share morphologic features with their **colonic counterparts**

Plaque-like, circumferential expansion of the mucosa by elongated, often dilated crypts with lateral branching or budding above the muscularis mucosae

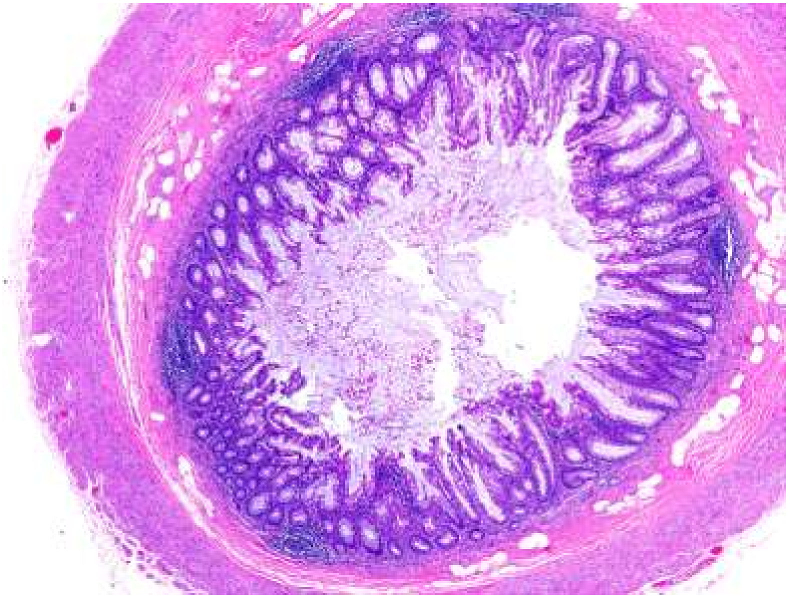
Mutually exclusive **BRAF and KRAS mutations are detected in near-equal numbers** of appendiceal SSLs, suggesting that they do not progress via the classic serrated neoplastic pathway of the colorectum



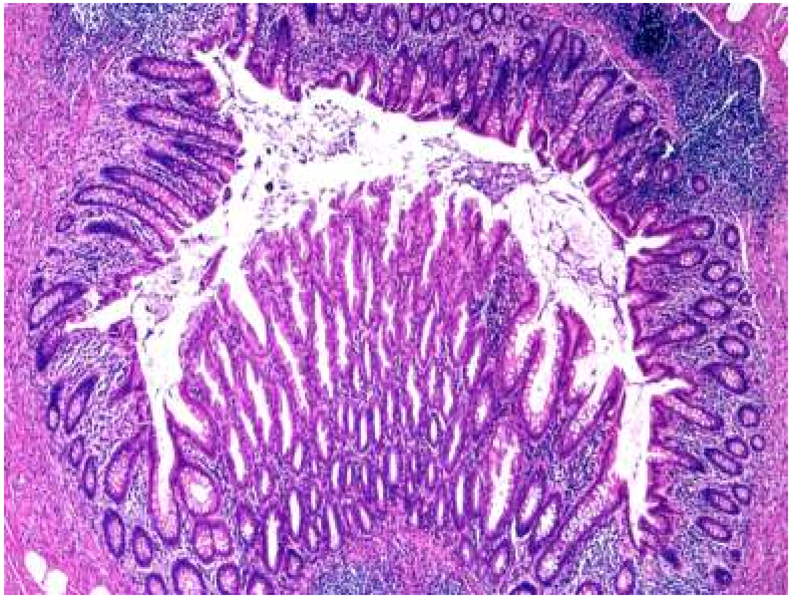




Sessile serrated neoplasm of the appendix



Serrated polyp
NOS



Serrated polyp
NOS

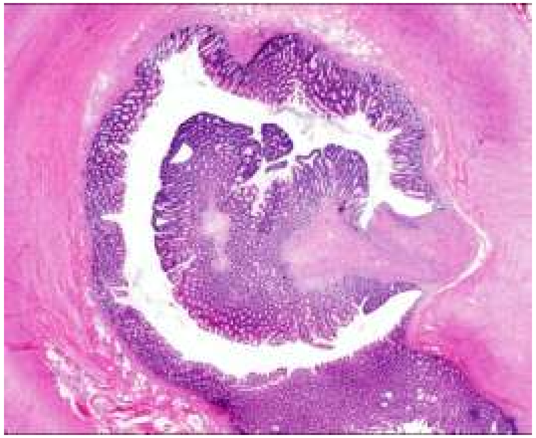
Conventional (colonic-type) appendiceal adenoma

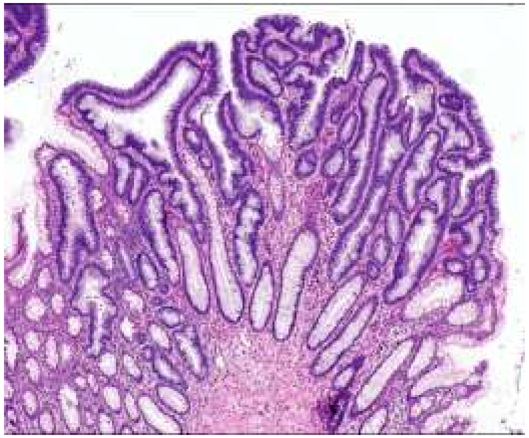
Resemble conventional adenomas of the colon

Detected in appendicectomy specimens

Some represent extension of cecal adenomas

Do not involve the full circumference of the lumen



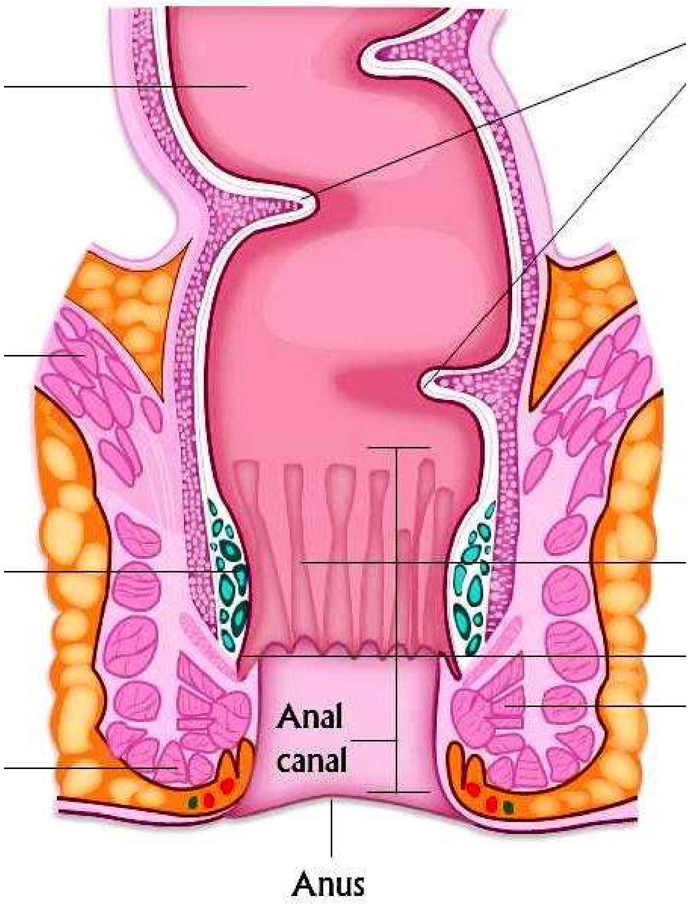


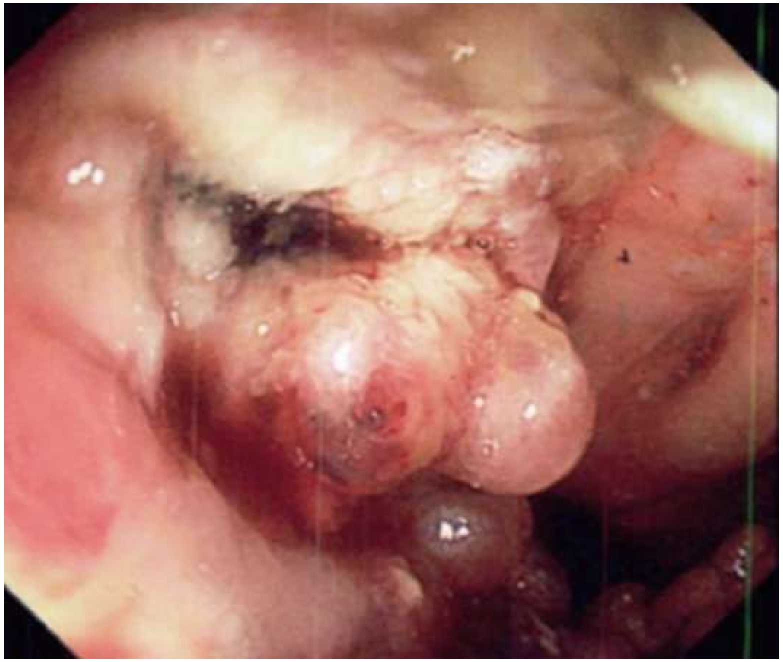
Benign epithelial tumors and precursors of the anal canal

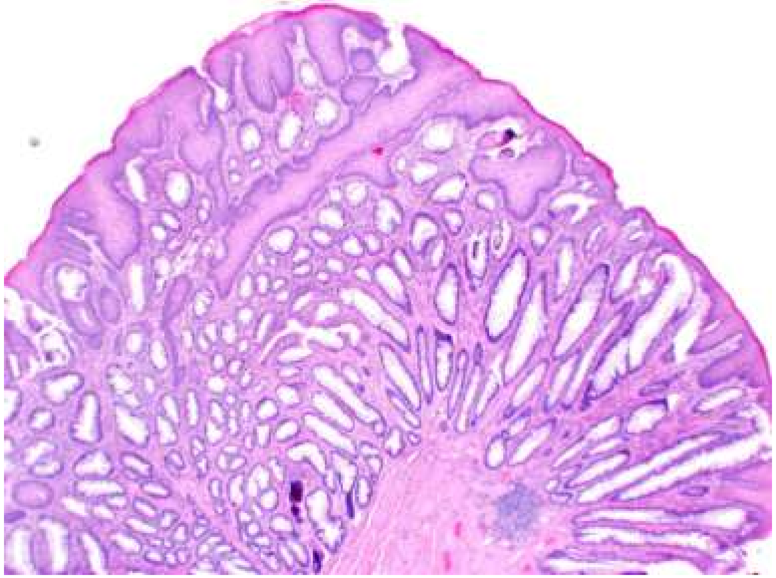
Inflammatory cloacogenic polyp

Anal condyloma

Anal squamous dysplasia (intraepithelial neoplasia)







Inflammatory cloacogenic polyp (ICP)

Non-neoplastic polyp

Arises in the **anal transitional zone**

Inflammation and glandular and smooth muscle proliferation

Related to a **low-fiber diet** (increase intraluminal colonic pressure)

Similar to mucosal prolapse syndrome (solitary rectal ulcer syndrome, rectal prolapse and proctitis cystica profunda)

Does not recur after removal

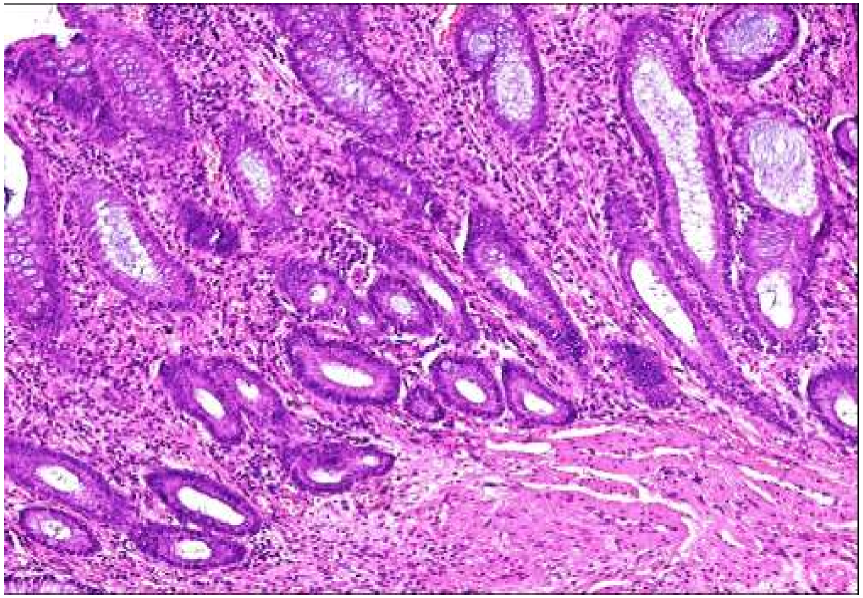
Inflammatory cloacogenic polyp

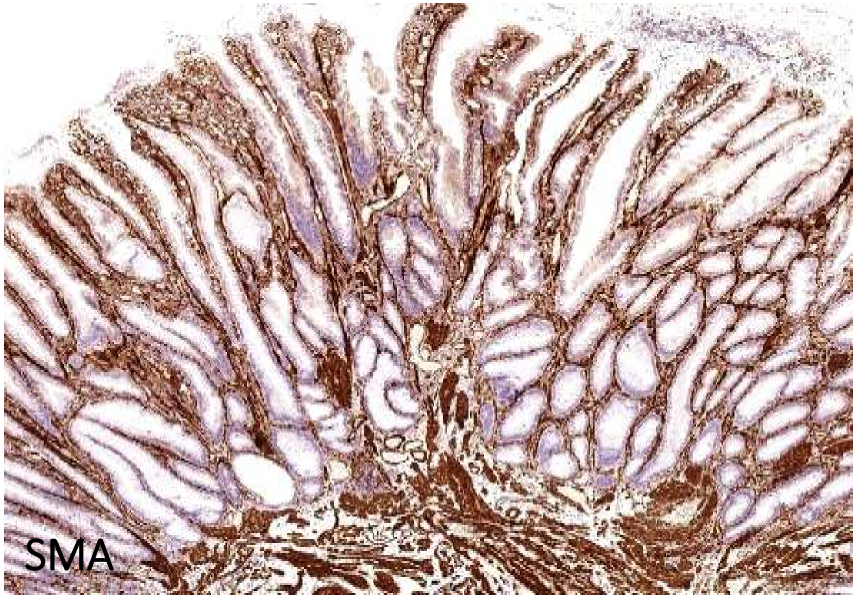
Covered by **hyperplastic epithelium** (squamous, columnar or transitional)

Complex **tubulovillous growth** with cystic change

Active chronic **inflammation, granulation tissue, vascular ectasia and oedema**

Fibromuscular proliferation and obliteration of the lamina propria in a radial fashion





Anal condyloma

Benign papillary **squamous proliferation** caused by **low risk HPV** subtypes HPV6 and HPV11

Buschke–Lowenstein tumor (BLT) is a giant condyloma with features of deep growth and local destruction

Condyloma occurs in the **anal canal, anal transformation zone, anal skin and perianal region**

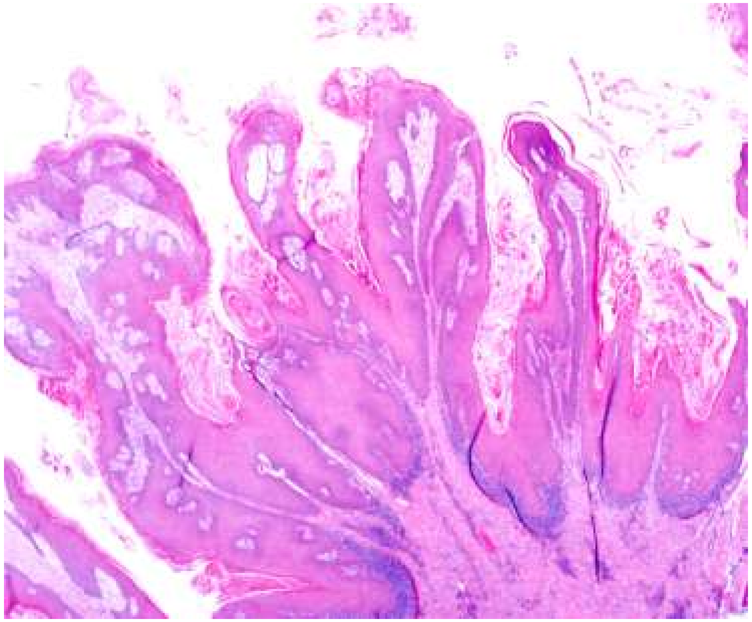
Anal condyloma

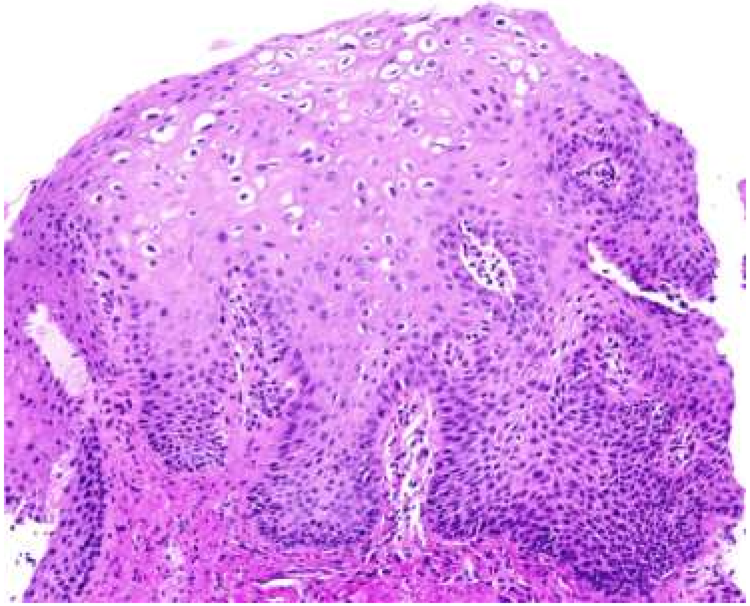
Squamous papilloma with **hyperplastic surface squamous epithelium with koilocytosis**

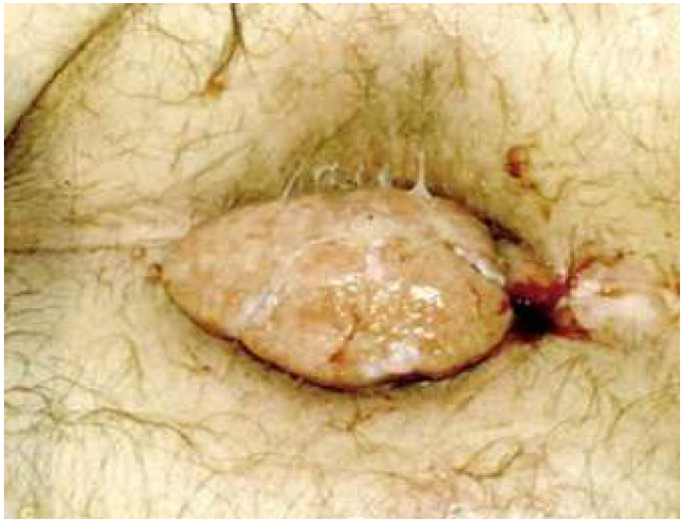
Large condyloma must be differentiated from verrucous carcinoma and BLT

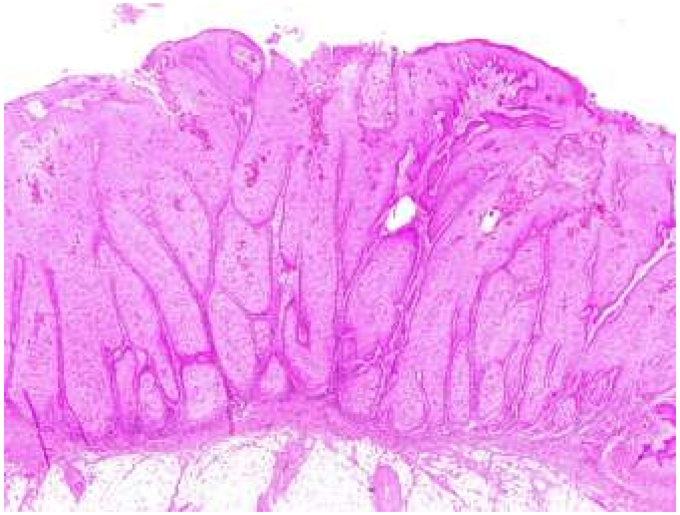
Small condyloma can regress and be treated conservatively

Large condyloma and BLT do not regress spontaneously and are prone to recurrence and malignant transformation





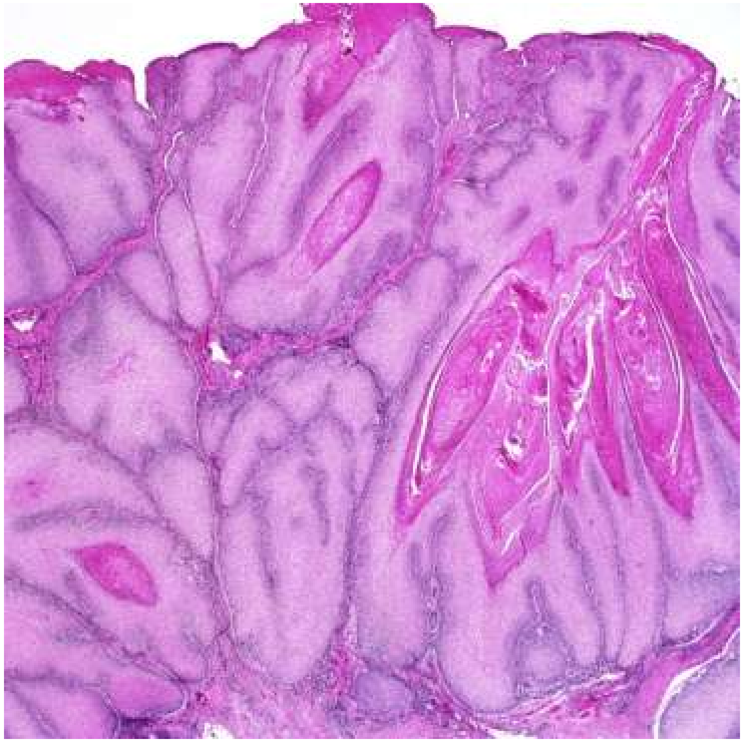




Verrucous Squamous Cell Carcinoma (VSCC)

VSCC is a **well-differentiated** variant of SCC primarily occurring in the **oral cavity, with additional sites including larynx, esophagus, anogenital region and sole of the foot**

Strong correlation with **tobacco and alcohol use** but relationship with **HPV,** though both low-risk and high-risk types have been **identified**



Verrucous Squamous Cell Carcinoma (VSCC)

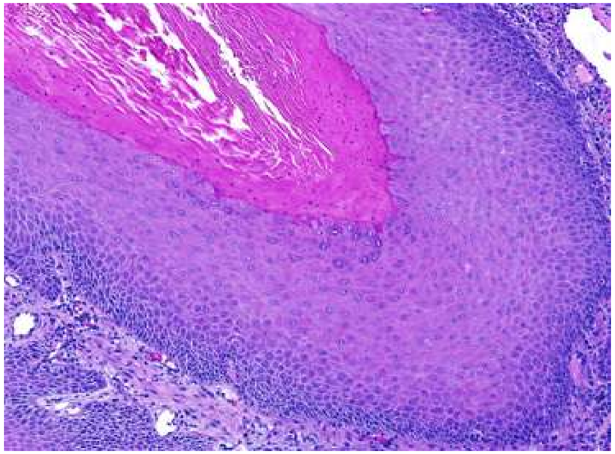
Present as **warty, cauliflower-like exophytic mass**

Well-differentiated SCC in large, rounded pushing nests with both exophytic and endophytic and endophytic growth patterns

Tumour cells show abundant, 'glassy' eosinophilic cytoplasm with lacks cytological atypia.

Club-shaped or "elephant foot-like" projections with peripheral cup formation and Intact basement membrane are characteristic

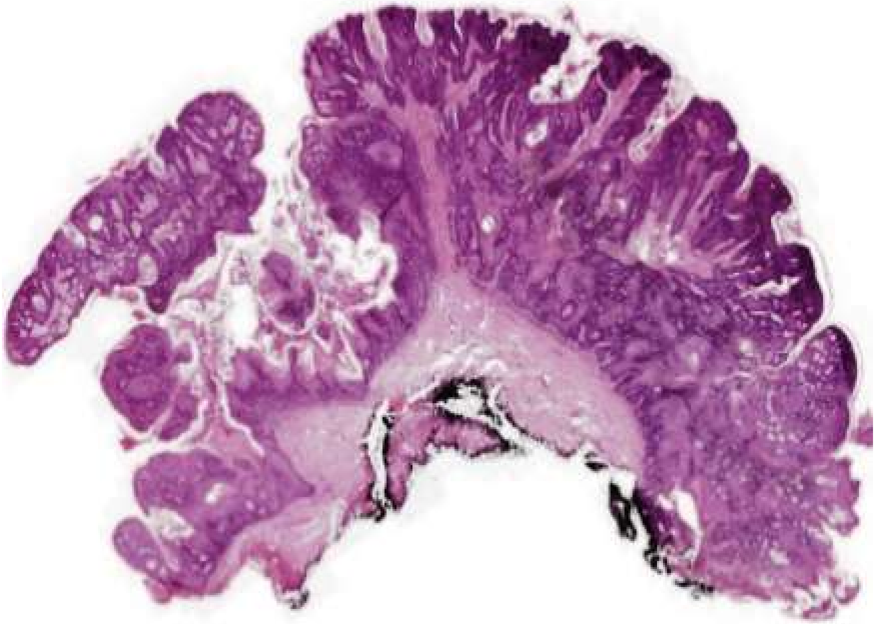
Surface shows marked epithelial hyperplasia with filiform projections



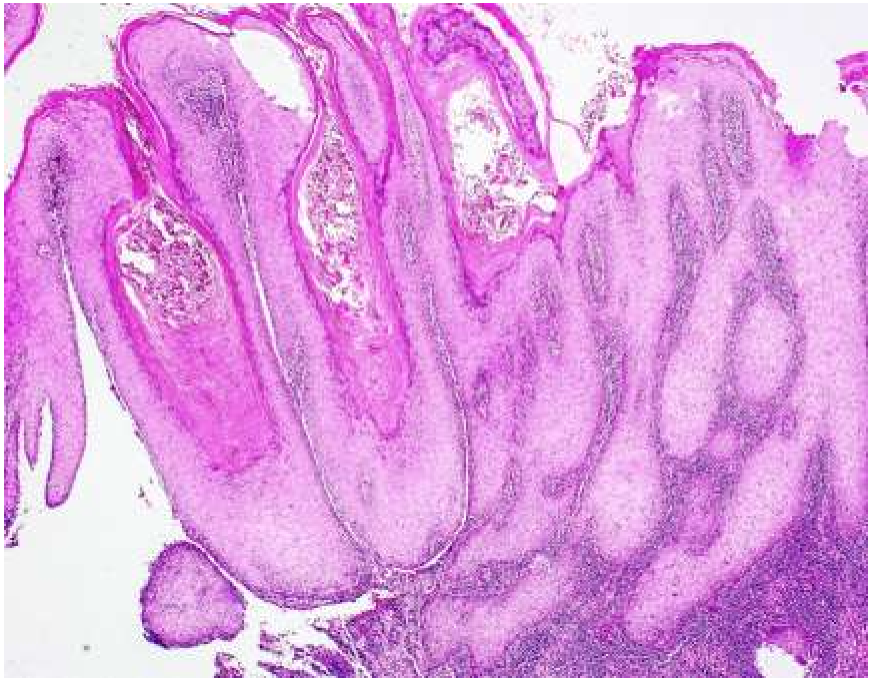
Diagnostic Criteria:
- Surface maturation
- Minimal/absent pleomorphism
- Rare to absent mitoses
- Inflammatory infiltrate at advancing edge

Variants:
- 20% may show conventional invasive SCC (keratinizing type)
- 10% show clear pleomorphism, requiring reclassification as conventional SCC

Differential Diagnosis:
- Verrucous hyperplasia
- Keratosis of uncertain significance
- Verruca vulgaris
- Squamous papilloma
- Proliferative verrucous leukoplakia
- Pseudoepitheliomatous hyperplasia
- Papillary SCC



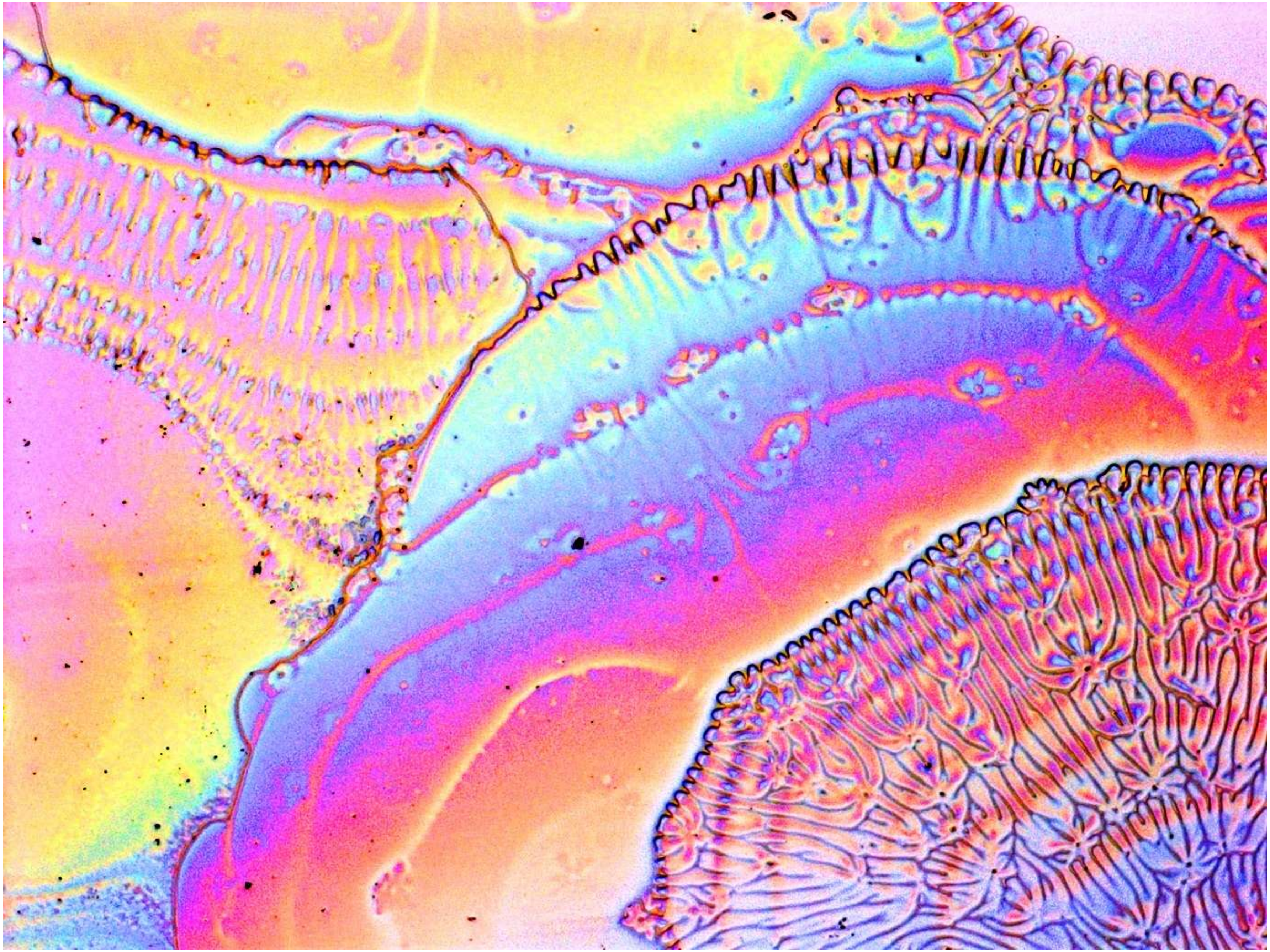
Anal condyloma



Anal verrucous carcinoma

Immunohistochemical characteristics of anal lesions

Tumour	Immunohistochemical markers					Other positive markers
	Pancytokeratin	CD45	S100	p40	Polyclonal CEA	
Anal squamous cell carcinoma	+	–	–	+	–	High-risk HPV in situ hybridization, p16
Basal cell carcinoma	+	–	–	+	–	Diffuse BerEP4
Neuroendocrine carcinoma (NEC)	+	–	–	–	Typically –	Chromogranin, synaptophysin, INSM1
Melanoma	Typically –	–	+	–	–	Melan-A, HMB45, SOX10
Extramammary Paget disease	+	–	–	–	+	GCDFP-15, GATA-3
Prostatic carcinoma	+	–	–	–	–	PSA, PSAP, NKX3-1
Colorectal carcinoma	+	–	–	–	+	CK20, CDX2, SATB2
Malignant lymphoma	–	+	–	–	–	PAX5 (often high-grade B-cell lymphoma)

Polyps of the colorectum

- Serrated polyps
  - Hyperplastic polyp
    - Microvesicular
    - Goblet cell-rich
    - Mucin-poor
  - Sessile serrated lesion/polyp
  - Sessile serrated polyp with dysplasia
  - Traditional serrated adenoma
- Adenomatous polyps
  - Tubular adenoma
  - Tubulovillous adenoma
  - Villous adenoma
- Hamartomatous polyps
  - Juvenile polyp
  - Peutz-Jeghers syndrome
  - Cowden syndrome
- Inflammatory polyps
  - Inflammatory pseudopolyp
  - Inflammatory cap polyp
  - Mucosal prolapse syndrome
- Miscellaneous
  - Inflammatory fibroid polyp (IFP)
  - Inflammatory myofibroblastic tumor (IMT)